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THE RELATION BETWEEN MALNUTRITION AND NERVOUSNESS

PART I *

MAX SEHAM, M.D.
AND
GRETE SEHAM, PH.D.
MINNEAPOLIS

Modern clinical medicine owes its growth and development chiefly to two philosophies of disease. The first of these which today dominates medical thought and practice, is known as the mechanistic; the second, in vogue for only about fifteen or twenty years, is known as the functional point of view. According to the former, any derangement in function of the organs of the body sufficient to cause symptoms and signs of disease must be due to definite change in structure or size of the tissue cells. Famous discoveries in pathology as those by Virchow, epoch-making contributions in biology as those by Darwin, and experimental data collected by such great physiologists as Helmholtz, Bernard, Liebig and Müller made only more pronounced the leaning of the medical profession toward mechanical interpretations of disease.

It is, therefore, not surprising to find the literature on the subject of nutritional disturbances most comprehensive in the description and discussion of the chemistry and pathology. We find that Jackson,[1] McCollum[2] and Morgulis,[3] in their respective textbooks explore thoroughly the fields of pathology and chemistry. Clinical treatises such as those by Emerson,[4] Holt,[5] Baker and Roberts[6] also betray

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* This work was assisted by a research grant given by Dr. Guy Stanton Ford, Dean of the Graduate School of the University of Minnesota.

1. Jackson, C. M.: The Effects of Inanition and Malnutrition upon the Growth and Structure, New York, The Macmillan Company, 1926.

2. McCollum, E. V., and Nina Simmonds: The Newer Knowledge of Nutrition, New York, The Macmillan Company, 1925.

3. Morgulis, Serge: Fasting and Undernutrition, New York, E. P. Dutton & Company, 1923.

4. Emerson, W. R. P.: Nutrition and Growth, New York, D. Appleton & Company, 1922.

5. Holt, L. E.: Food, Health and Growth, New York, The Macmillan Company, 1923.

6. Roberts, Lydia: Nutrition Work with Children, Chicago, Univ. Chicago Press, 1927.

the purely mechanistic point of view. It is hardly an exaggeration to say that the literature on this subject as it relates to dynamic and behavioristic physiology is meager, and that the clinical writings abound with subjective opinions which time has allowed to assume the character of traditions.

The term malnutrition has both a popular and a scientific usage. In infancy it has reference to alimentary disturbances in which there is an inability to digest and assimilate foods necessary for proper growth and development. It is known as infantile atrophy, athrepsia, marasmus and decomposition (German classification). In the older child, it has, through popularization, acquired the meaning of a state of undernutrition in which the body weight is 7 per cent, or more, below the average weight for the average height for a given age. Such a definition immediately makes clear the point of view of its advocates. It is of no consequence whether the state of nutrition is the primary result of inadequate food habits or the secondary result of organic disease or foci of infection. Here then malnutrition is only one of many symptoms and is secondary to physical disease. It should be therefore termed secondary malnutrition.

Primary, or essential malnutrition, on the other hand, is an entity representing a state of disturbed nutrition which is usually due to inadequate health habits, especially food habits, and which is associated with a depression in activity (fatigue syndrome) or an excess in activity (nervous syndrome) or both, with loss in body weight as a common, though not necessary, sign. We realize, of course, that it is difficult to draw a sharp line of demarcation between normal and abnormal nutrition. Nutrition is the process which governs not only the form, size, structure and maintenance of the bodily tissues and organs, but also their functional interactions. It is the nutritional process on which proper correlation and perfect harmony of the workings of the various physiologic systems depend.

Good nutrition, one might say, is characterized by adequate action of the internal organs, a stable nervous system, good posture, sufficient muscular strength and endurance, well-functioning special senses and good inhibition and coordination.

Since, during the last ten years, the weight and height index has apparently been accepted as the chief and often the only diagnostic standard of malnutrition, it might be in place to discuss this factor more fully. The two weight-height indexes most in vogue in this country have been devised by Holt-Burk-Boas and by Baldwin-Wood. The former is based on the height and weight measurements of many thousand children of the poorer classes in New York City. Weight and height are correlated without reference to age. The Baldwin-Wood tables are computed from similar measurements of a selected group of

children attending private schools. Here the weight is correlated with height and age. The difference in the selection of subjects for the two standards accounts for the discrepancy of from 1.2 to 6 pounds (0.6 to 2.7 Kg.) for children of the same age.

The two chief criticisms against the diagnostic use of the height and weight index are, (1) the assumption that it determines with fair accuracy the nutritional state of every child, and, (2) the arbitrary fixation of a 7 or 10 per cent line of demarcation between good and poor nutrition. That this index is not sufficiently reliable is shown by Robertson who found the normal variability for children of the same age to be from 10 to 20 per cent in weight and of from 4 to 6 per cent in height. Furthermore, racial and social differences affect weight as well as height. Neither experimental nor statistical evidence has been offered in the medical literature to show why 7 or 10 per cent below the average weight for height for a given age should be accepted as diagnostic of poor nutrition. It can be safely said that unless the height and weight index is used merely as an aid and not as the chief or only basis for the diagnosis of malnutrition, its usefulness will be discredited in the near future.

RELATION BETWEEN NUTRITION AND FUNCTION

It is a well established fact that depending on the kind and duration of inanition, the body suffers a more or less severe loss in weight. If food is withdrawn or, for some other reason, normal digestion and assimilation are interfered with, the body falls back on its own reserves of fat for the maintenance of its proper nutritional processes and functions. In order to maintain the body temperature, to perform the vital functions of the heart, lungs and secretions and to produce mental and physical work, there results either a compensatory depression or an excess of function commonly known as fatigue and nervousness. It is a moot question whether functional disturbances precede or follow pathologic changes. The latter have been well studied in animals, while the former are still awaiting investigation.

Lee and Morgulis studied the effect of inanition on the activity of the diaphragm and extensor cruris muscles in starved cats. They observed a decrease in their working capacity of from 30 to 40 per cent when the loss reached from 10 to 19 per cent of the original weight, and of one-half when the loss amounted to from 30 to 40 per cent. It is of interest to note that depletion in activity of an individual muscle is not, as one might expect, accompanied by a reduction in the total output of the animal's activity. In fact, toward the end of the fast, in the extreme stages of emaciation, these animals increased their total activity considerably.

It has also been observed that the central nervous system shares in the general loss of weight. This is due to atrophy of the ganglion cells of the brain and of the cord.

Furthermore, during the last stages of inanition, the cells of the spinal cord undergo vacuolization, turbidity, pigmentation and granulation. But whether the pathologic changes in man occur in the brain or in any other part of the nervous system, we have not yet learned. It is, therefore, difficult to explain the nervous symptoms and functional disorders which manifest themselves even during the first few days of total or partial inanition and in the early stages of malnutrition.

In this regard the theory advanced by Lydia Roberts is worth quotation:

> The rapidly developing brain and nervous systems of the child require certain essential food materials for normal growth. Moreover, the nerves need a moderate covering of fat to protect them from external stimulation. In a malnourished child, both of these conditions for a normal nervous condition are apt to be lacking, the food materials more than likely being deficient and the nerves unprotected owing to the lack of subcutaneous fat.

This is an interesting explanation of the functional disorders accompanying malnutrition but we have been unable to find any experimental data to justify such a statement.

Holt, in a clinical study, divides malnourished children into the following two groups: (1) the dull, the listless, the easily fatigued; and (2) the hyperactive, the excitable, the irritable and the hyperkinetic. He goes so far as to ascribe all nervous symptoms such as headaches, insomnia, habit spasm and even chorea—experimental evidence has never substantiated this claim—to nutritional disorders. Blanton[7] has also noticed functional disorders in children suffering from malnutrition. The war offered him the opportunity to study 6,500 German children in the city of Trier, Germany. Their food intake had been limited to 1,400 calories—about one-half their normal needs. His article is illuminating as an example of how undernutrition will produce restlessness, inability to sit still and misbehavior on the one hand, and fatigue and reduced muscular strength and endurance on the other hand.

To make an accurate study of the effect of nutritional disorders in the child is most difficult, because it is practically impossible to control all the factors involved. In the animal, however, cause and effect can well be kept under control. In order to study the relationship between malnutrition and activity, it seemed therefore advisable to limit the experimental study to work with animals.

EXPERIMENTAL STUDY

Twenty male rats in good health and of the same age were selected. Throughout the experiment, each rat was kept in a revolving cage equipped with a

7. Blanton, Smiley: Ment. Hyg. **3**:343, 1919.

pedometer for recording the number of revolutions per day. The readings were taken before feeding at the same hour every day. Each rat was weighed before feeding at the same hour of day. For eighteen days, the rats were fed bread soaked in milk and a bucket of growing chicken mash diluted with skimmed pasteurized milk. At the end of that period, the diet was reduced to the mash for ten rats, the remaining ten rats continuing on the previous diet for control.

All but one (rat 4) of the ten rats subjected to this reduced diet, lost considerably in weight. The duration of underfeeding varied from fourteen days (rats 1, 2 and 5) to eighteen days (rats 6, 7, 8, 9 and 10). One rat (rat 3) succumbed after nine days. In rat 4 the experiment was extended to twenty-one days Here the food ration was further reduced on the tenth day to three fourths of the quantity used at the beginning of inanition, to one half on

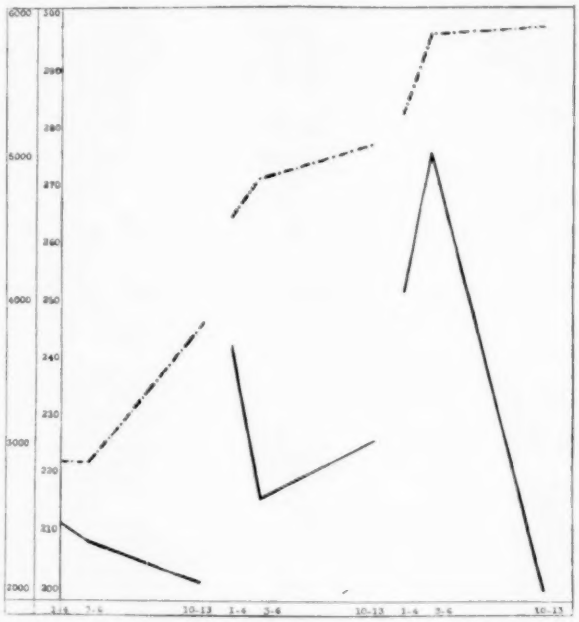


Fig. 1.—The activity and weight of control rats are shown in figures 1 to 10 inclusive.

the fourteenth day and to one fourth two days later. The rat died two days after the final reduction in food.

ANALYSIS OF RESULTS

The measurements of activity and weight for the first four days were omitted. The curves showing the activity and weight of the control group are shown in figures 1 to 10; those of the rats subjected to malnutrition in figures 11 to 20. On the ordinate are plotted the number of revolutions (farthest column to the left) and the weight in grams. The figures on the abscissa designate the number of days. Instead of recording activity and weight day by day, their average

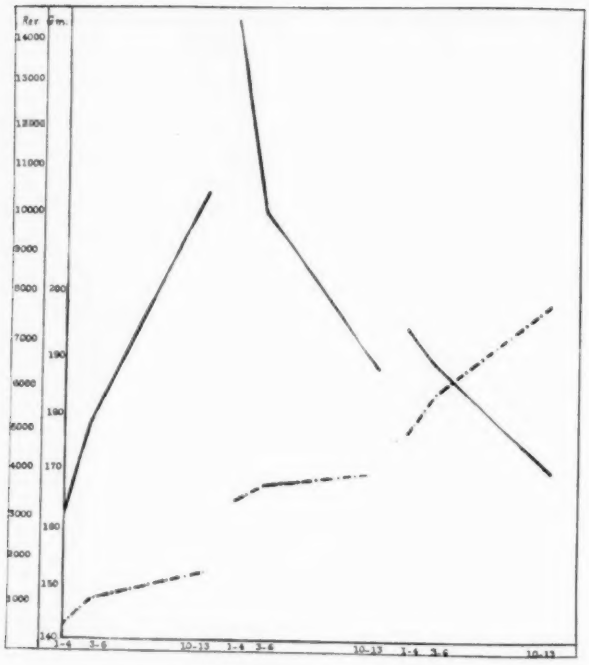


Figure 2

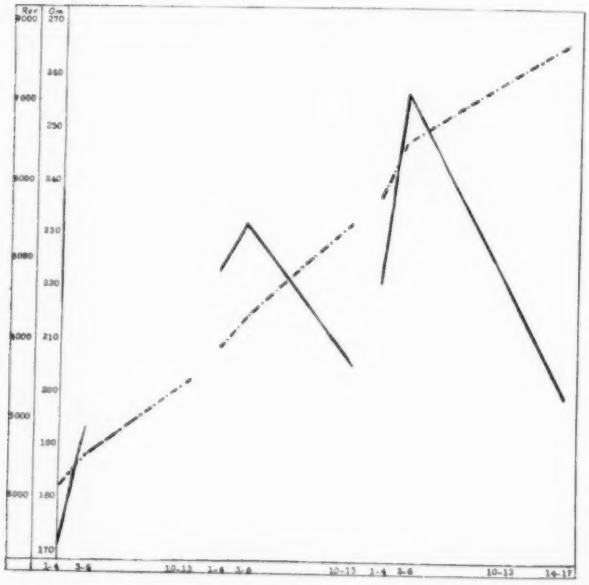


Figure 3

was calculated for the first four days, for the third to the sixth day, for the tenth to the thirteenth day, and for the fifteenth to eighteenth day, respectively.

The experiment was divided into three periods: (1) the period of preinanition, (2) of inanition and (3) of postinanition. During the process of inanition, rat 1 tripled his activity, the loss of weight being 14.6 per cent. Rat 2 did about ten times as much as before with a loss

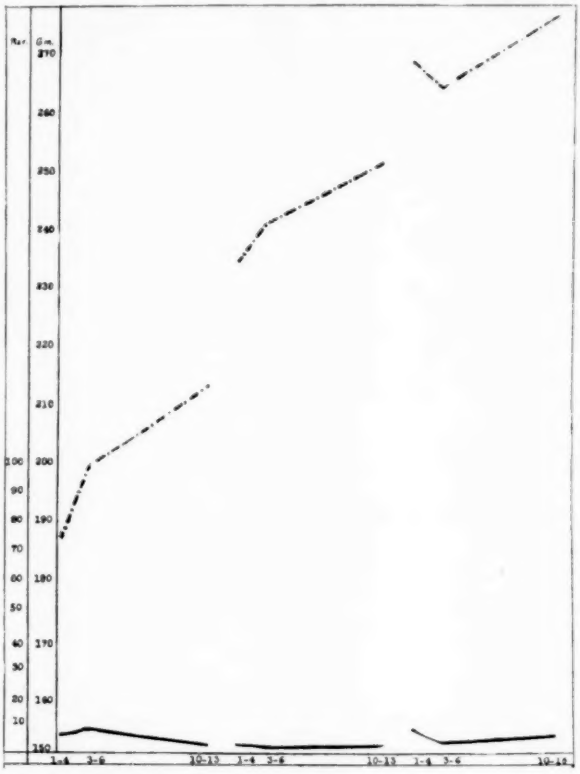


Figure 4

in weight of 22.4 per cent. Rat 3 showed on the fourth day the first extremely high record—eight times that of the preinanition activity; he then continued on this high level of activity until death. Two days before death his activity had risen to fifteen times the original amount, with a loss in weight of 15 per cent. At the time of his death his loss in weight had risen to 21.6 per cent.

In rat 4, on the other hand, malnutrition was produced only with difficulty; he was a lazy rat, his median daily activity amounting to only 8 revolutions. On the seventeenth day the loss of weight was

9.4 per cent, the food supply was then further decreased to only a half tablespoonful of mash a day. The activity increased to 44 revolutions on the nineteenth, and to 799 on the twentieth day. The rat died during the following night, with a loss in weight of 28.5 per cent.

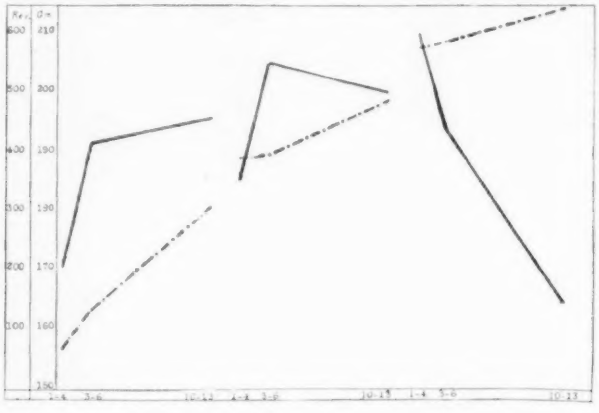


Figure 5

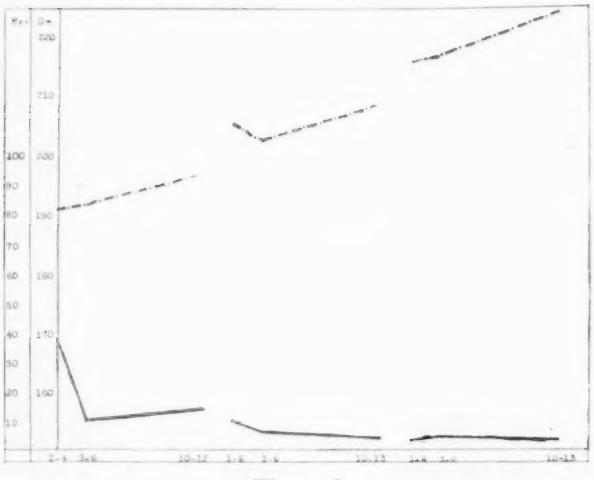


Figure 6

In rat 5, the final increase in activity was ten times the original amount, with a loss in weight of 16 per cent.

Rat 6 was also a lazy rat. His activity, however, already had risen in the ninth day from about 7 revolutions to 400. The average for the tenth to thirteenth day amounted to almost 1,000 revolutions, with a final loss in weight of 7.8 per cent.

Again, in rat 7, the final increase in activity was 250 times that of the preinanition record—from 9 to 2,227 revolutions—and his loss in weight was 13.3 per cent.

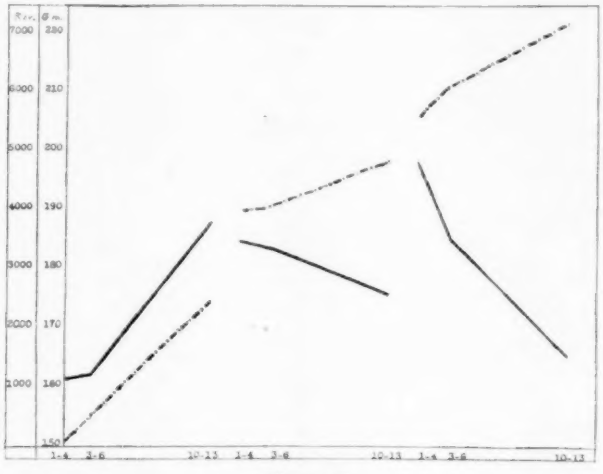


Figure 7

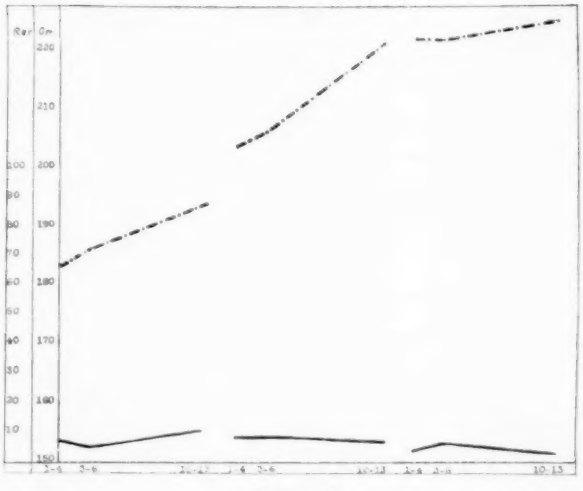


Figure 8

Rat 8 increased his daily activity from 150 to about 3,000 revolutions. Rat 9 changed from an average of 6 to about 600 revolutions per day and lost 12.2 per cent in weight. Rat 10, on the other hand, increased his rate during only the later stage of inanition (ten times the original amount); his loss in weight was 16.7 per cent.

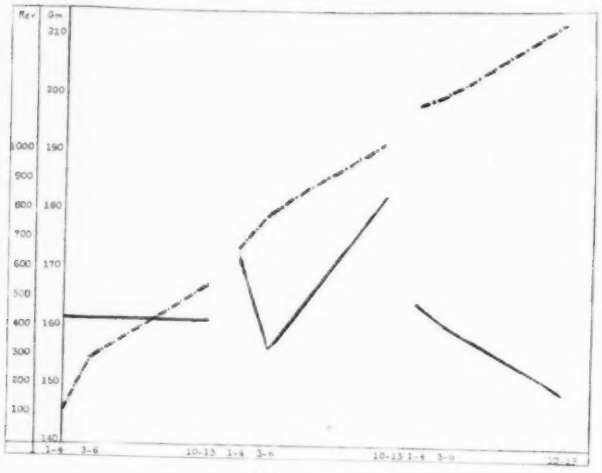


Figure 9

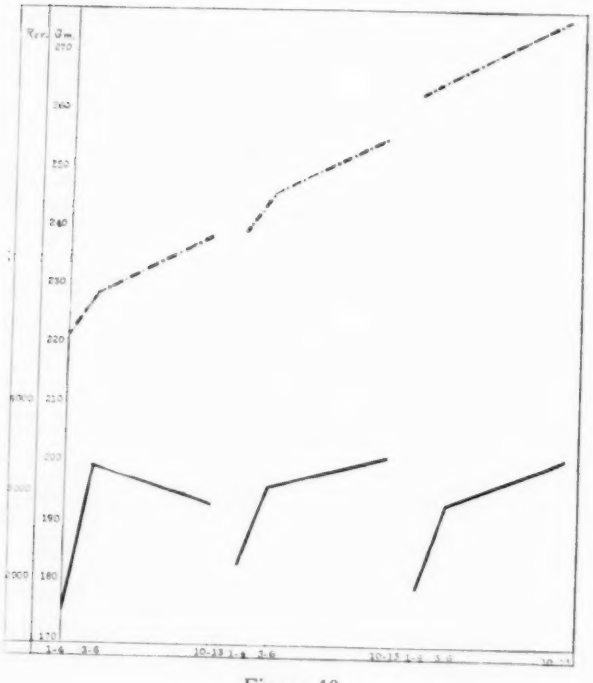


Figure 10

An analysis of the foregoing data might give the impression that the average percentage loss in weight is not in proportion to the activity performed. There is no basis, however, for calculating this relation, since some rats increased their activity at the onset of inanition, while others showed a considerable increase in activity during only the later if not the last stage of inanition.

The figures also reveal that as soon as the animal is put back on a diet adequate for its normal growth, the activity begins to drop and the weight rises again. Such definite changes in activity cannot be

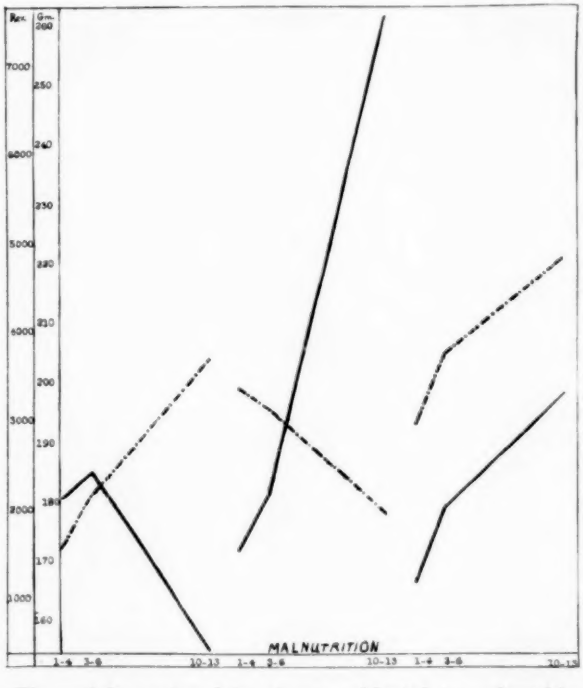


Fig. 11.—The activity and weight of rats subjected to malnutrition are shown in figures 11 to 20 inclusive.

found in the control rats whose activity fluctuates only within normal limits. One is, therefore, justified in concluding that hunger is a cause of activity.

RELATION BETWEEN ACTIVITY AND LOSS OF WEIGHT

Two methods of calculation were used to establish whether loss of weight in the malnourished rats was due only to lack of food or also to the amount of work performed.

The first method consisted in calculating the midamount (median) of the daily activity and of the daily weight. (The midamount of a

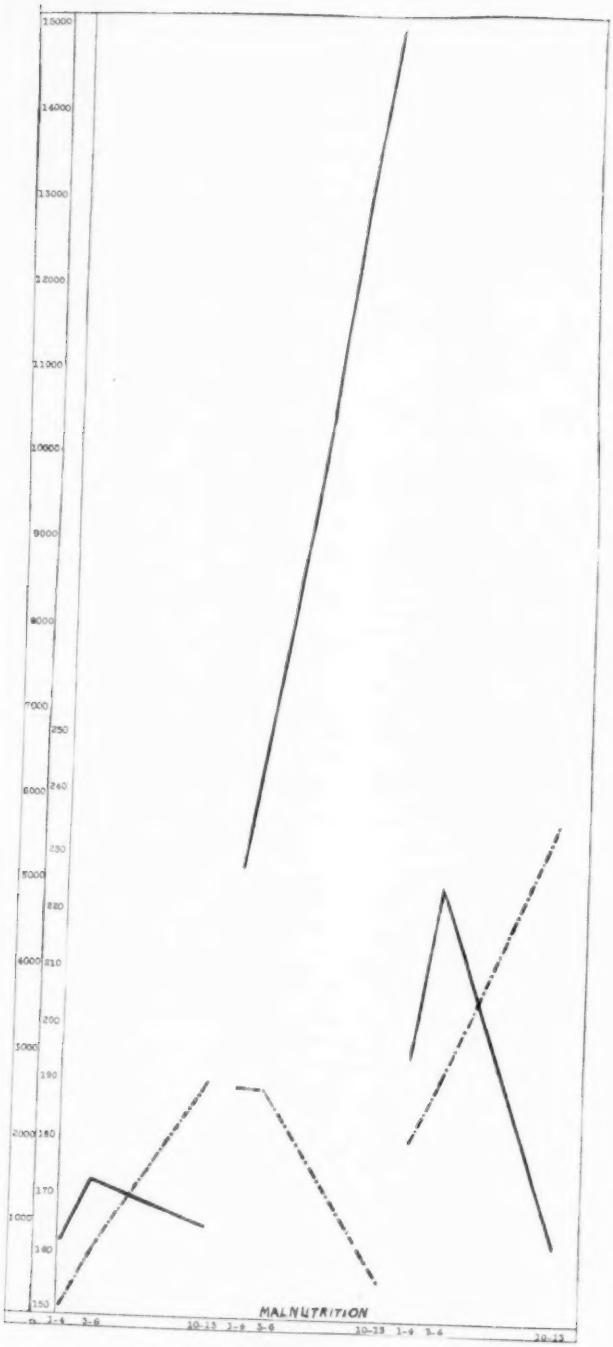

15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
250
240
230
220
210
200
190
180
170
160
150
MALNUTRITION

Figure 12

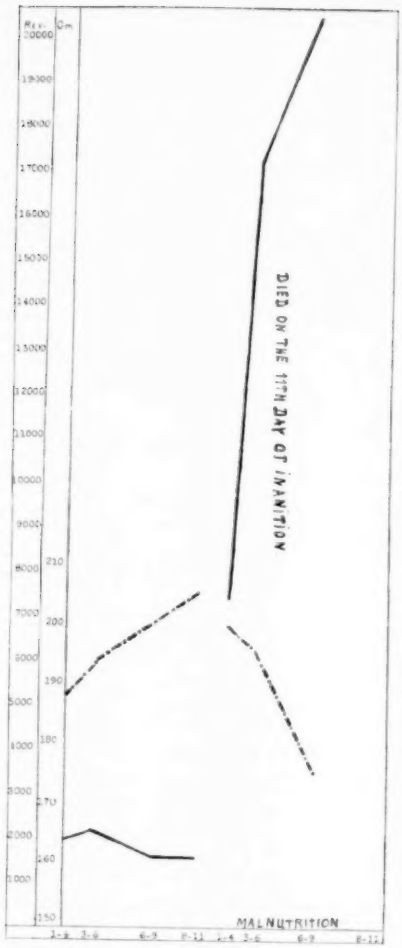


Figure 13

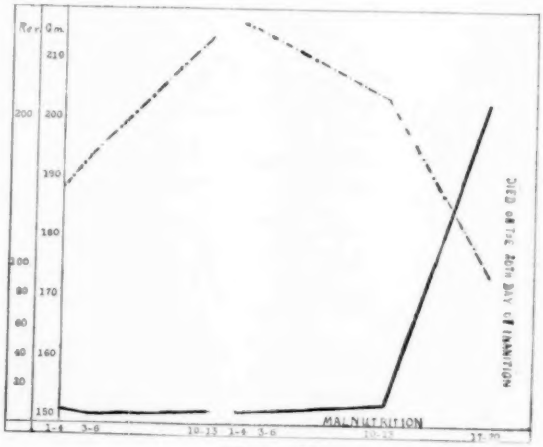


Figure 14

series is the value of the midmost measure; hence half the measures composing the series lie above it and half below it). The following example is used to illustrate the procedure. Suppose rat O has the following record of activity:

Number of days	Activity in Revolutions	Weight in Grams
1	200	150
2	300	148
3	250	151
4	400	152
5	220	155
6	260	151
7	500	146
Midamount	260	151
Above the midamount	300	151
	400	152
	500	155
Below the midamount	200	146
	220	148
	250	150

To make the relation between these two factors positive, in the majority of cases, an activity above the midamount should be followed by a weight below the midamount, or activity below the midamount should be followed by a weight above the midamount. If the midamount activity corresponds with the midamount weight, the relation is also considered positive. One then finds such a relation to exist on the second, fifth, sixth and seventh days, that is, in four of seven cases there is a positive relation between activity and weight the following day.

TABLE 1 *A.—Relation Between the Amount of Activity and Loss in Weight*

	Control				Malnutrition			
	First Two Weeks		Second Two Weeks		First Two Weeks		Second Two Weeks	
Cases	Group A*	Group B‡	Group A	Group B	Group C	Group D	Group C	Group D
1	5+	5	9+	0	6+	5	6+	3
2	6+	3	7+	4	8+	3	4	5
3	6+	4	8+	2	4+	2	..	..
4	9+	4	5	6	13+	4	..	..
5	6+	4	7+	4	2	9	7+	2
6	6+	4	5	6	7	8	10+	2
7	5	5	8+	2	9+	5	5+	4
8	5	5	6+	5	11+	2	5	7
9	5+	4	5	6	7+	10	2	2
10	5+	3	8+	2	8+	..	5	6
Total positive	8 of 10		7 of 10		8 of 10		4 of 8	

* Figures marked with a plus sign indicate a positive relation between the activity and the gain in weight on the following day; that is, a higher activity is followed by a smaller gain or a larger loss in weight the following day. Thus in group A seven of ten cases substantiate the evidence that a definite relation exists between these two factors.

‡ Group B and group D: Number of cases in which the activity below the midamount was followed by a gain in weight below the midamount the following day or in which the activity above the midamount was followed by a gain in weight above the midamount the following day.

The data as yielded by this method are listed in table 1*A*. The upper half refers to the rats used for control, and the lower for the rats subjected to malnutrition. Groups *A* and *C* designate the number of measures in which the activity below the midamount was followed by a gain in weight above the midamount the following day, or in which the activity above the midamount was followed by a gain in weight below the midamount the following day. Groups *B* and *D* designate the number of measures in which the activity below the midamount was followed by a gain in weight below the midamount the following day; or in which the activity above the midamount was followed by a gain in

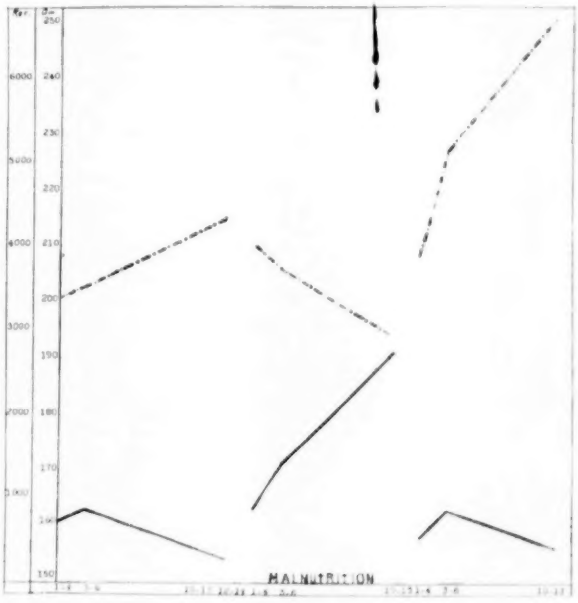


Figure 15

weight above the midamount the following day. Cases marked with a positive sign indicate a positive relation between activity and gain in weight, that is, the activity below the midamount was followed by a gain in weight above the midamount the following day; or the activity above the midamount was followed by a gain in weight below the midamount the following day.

Thus it is found that this relation is positive for the first and second two weeks in the control rats (eight and seven of ten cases, respectively), and for the two weeks of malnutrition (eight of ten cases). These results, therefore, suggest that the amount of activity is in positive relation to loss in weight. Additional evidence of a positive relation between activity and loss in weight was offered by another experiment

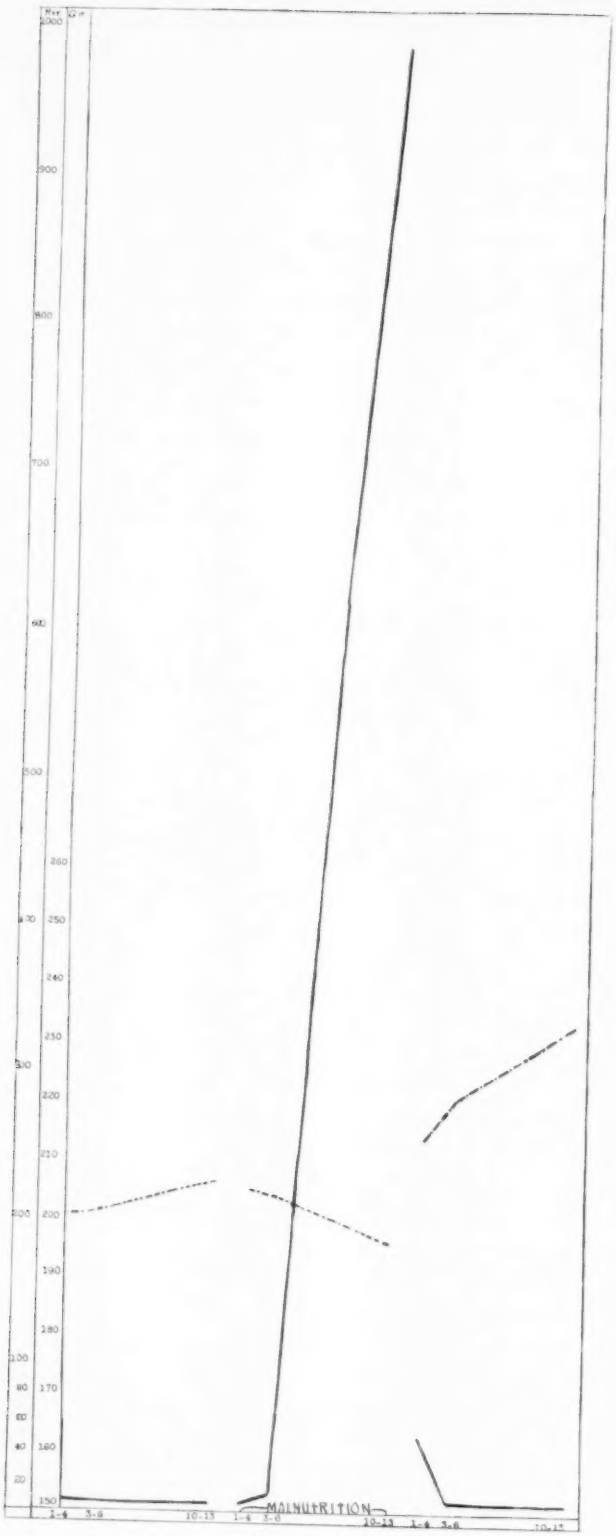


Figure 16

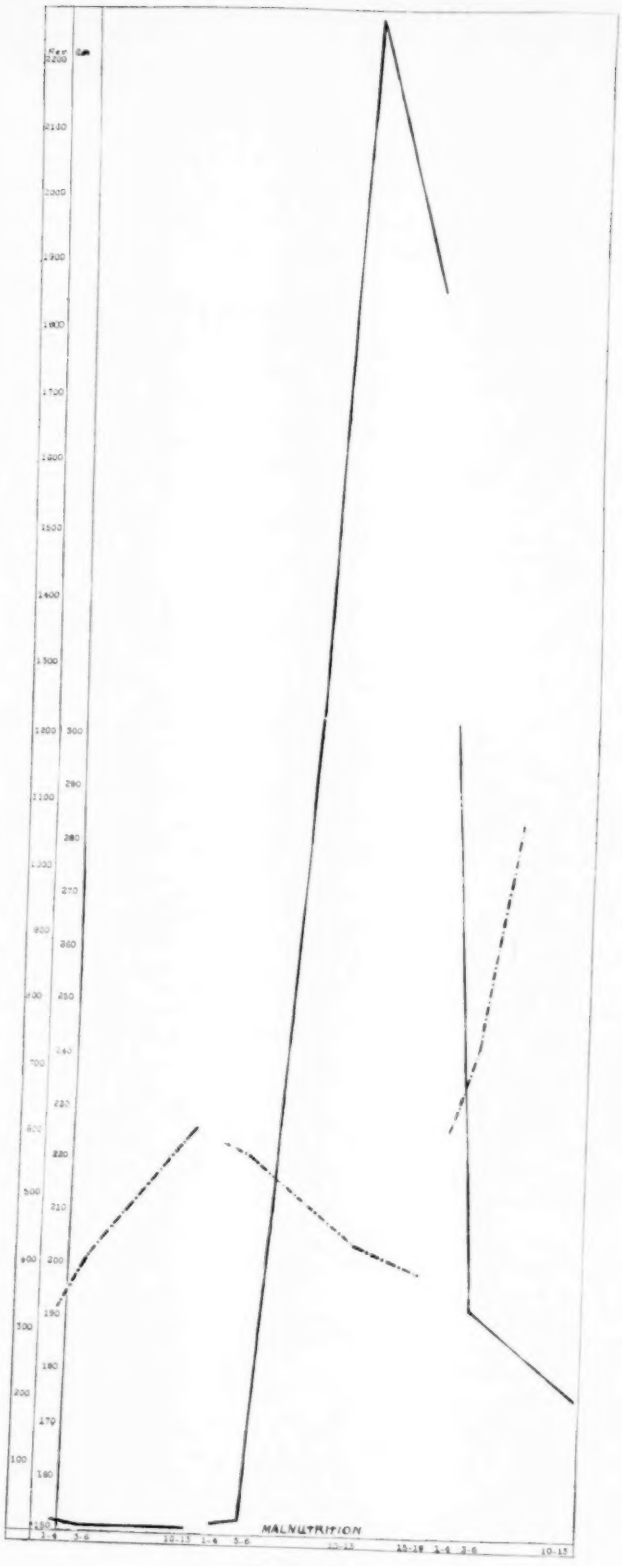


Figure 17

in which the effect of exercise on rats was studied. With an excess of food, always accessible to the rats, the loss in weight which they underwent can be accounted for by the forced activity. Furthermore, the rats showed a loss in weight immediately after activity was artificially produced. Further data on the effect of exercise on rats will be published in a later article.

The second method consisted in determining the number of times in which a higher activity was followed by a smaller gain in weight or greater loss the following day; or in which a smaller activity was followed by a greater gain in weight or smaller loss the following day. Again an example may help to make this method clearer. Suppose rat O shows the following records of activity and weight:

Day	Activity	Weight in Grams
1	200	150
2	300	148
3	250	151
4	400	152
5	280	155

As can be seen the rat weighs 150 Gm. after an activity of 200 revolutions. Higher activity the following day is followed by a loss in weight of 2 Gm. Let us designate this relation as positive. A smaller activity on the third day is followed by a gain of 3 Gm.; that is again a positive relation. On the fourth day a higher activity is followed by a gain; this, then, is a negative relation. A lower activity on the fifth day is followed by a greater gain; this relation is again positive.

In this example, then, in three of four cases a positive relation exists. Applying this method to the records showing the activity and weight of the control and malnourished rats, one finds that this relation is positive for the first two weeks (eight of ten cases), and the last two weeks in the control rats (seven of ten cases), and for the two weeks of malnutrition in the malnourished rats (eight of ten cases). The results are tabulated in table 1 *B*. Groups *A* and *C* have reference to the number of measures in which a higher activity is followed by a smaller gain or an actual loss in weight the following day.

Groups *B* and *D* represent the number of measures in which a higher activity was followed by a higher gain or a smaller loss in weight the following day. The case numbers with a plus sign indicate a positive relation between activity and gain in weight on the following day, that is, a higher activity is followed by a smaller gain or larger loss in weight the following day.

These results substantiate the evidence obtained by the first method, namely, that a positive relation exists between activity and gain or loss in weight the following day.

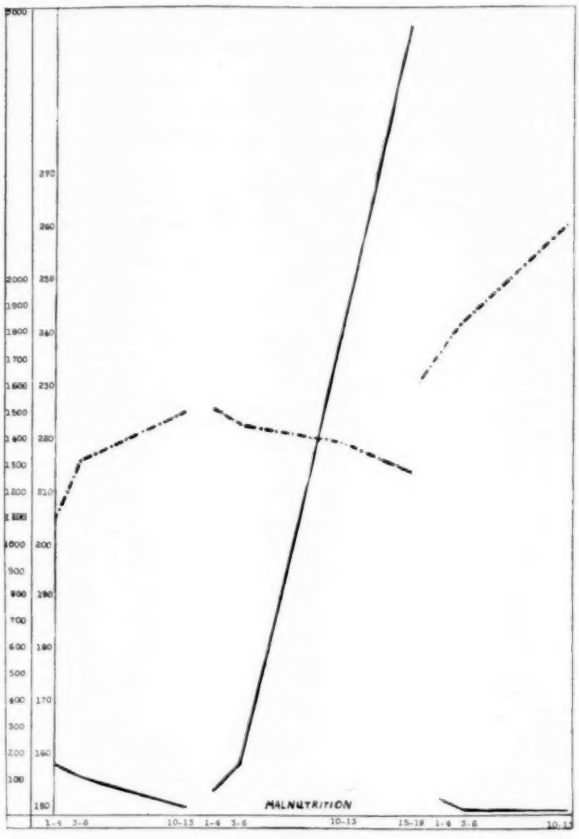


Figure 18

TABLE 1 *B.—Relation Between Amount of Activity and Loss in Weight*

	Control				Malnutrition			
	First Two Weeks		Second Two Weeks		First Two Weeks		Second Two Weeks	
Cases	Group A*	Group B	Group A	Group B	Group C	Group D	Group C	Group D
1	6+	..	5+	3	4	8	8+	2
2	6+	4	9+	3	8+	4	7+	3
3	6+	2	9+	2	4+	3	..	..
4	10+	6	6+	5	13+	3	..	..
5	5	4	8+	4	1	10	1+	4
6	4	6	6+	5	10+	5	9+	1
7	9+	2	9+	2	7	8	6+	4
8	4	5	5	6	6+	1	5	6
9	7+	6	5	7	9+	6	1	4
10	5+	2	7+	5	8+	1	7+	5
Total positive	7 of 10		8 of 10		7 of 10		6 of 8	

* Group A and group C: Number of cases in which the activity below the midamount was followed by a gain in weight above the midamount the following day or in which the activity above the midamount was followed by a gain in weight below the midamount the following day.

The experimental data here discussed can be summarized as follows: 1. Hunger is the cause of increased activity. 2. There is strong evidence that a positive relation exists between activity and loss in weight.

CLINICAL OBSERVATIONS

Coincident with loss in weight, general emaciation was observed which became more marked the more the rat lost in weight. This

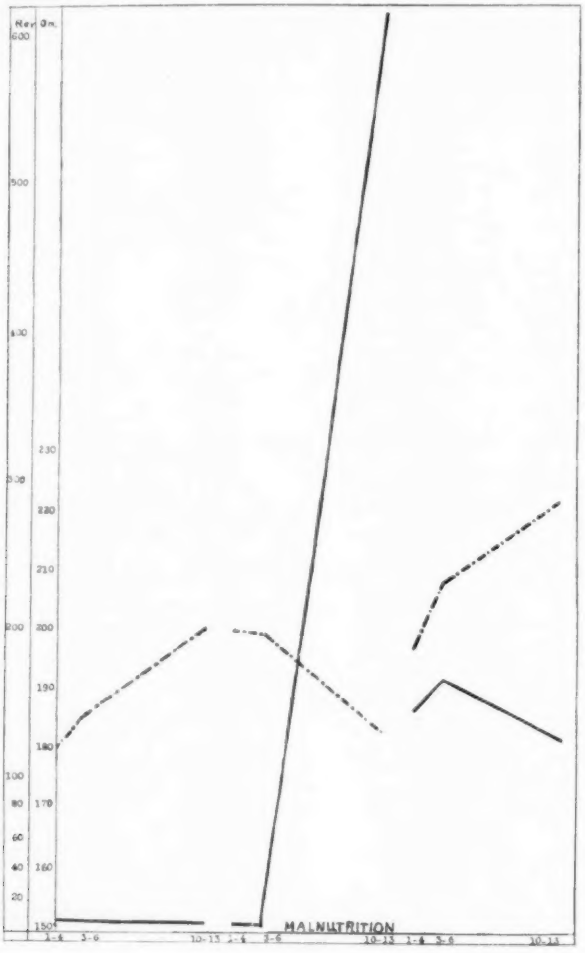


Figure 19

change from good to poor nutrition was especially noticeable, since, at the beginnings of the experiment, the rats were in unusually good physical condition. A few hours before death apathy and a decrease in body temperature set in. With the exception of rat 6, all the rats showed marked restlessness.

Table 2 shows the contrast in restlessness of the control and the malnourished rats. In the control group only rat 3 showed some restlessness which was also due to lack of food. Rat 8, also in that group, developed a peculiar twirling movement on the eleventh day. It disappeared on the twenty-fifth day. (This movement, peculiar to rats,

TABLE 2.—*Study of Restlessness in Rats*

	Control	Malnutrition		
	During 68 Days	Before	During	After
1		..	+	+
2		..	+	+
3	+ (lack of food)	..	++ died	
4		..	+++ died	
5		.	++	+
6		..	..	..
7		..	+	..
8	Twirled (11-25 days)	..	+	+
9		..	+	..
10	+ (after exercise)	..	+	+

TABLE 3.—*Comparison of Blinking in Rats*

		October												November										December					
	Rat	6	13	16	17	18	19	20	21	22	24	26	29	3	4	12	13	16	24	26	27	29	30	1	2	3	5	7	10
Control	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
	2	..	..	..	..	..	..	..	..	..	..	10	..	..	..	..	..	..	..	..	4	..	..	5	15	8	..	..	+
	3	..	..	..	..	..	..	..	..	..	4	..	..	10	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
	4	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	2	..
	5	..	..	..	..	..	..	..	..	..	3	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
	6	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
	7	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
	8	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
	9	..	..	..	..	..	..	..	..	..	..	2	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
	10	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	3	..	..	..	..	..	..	..	..	..	..	..
Exercised	1	..	..	..	..	..	..	..	..	..	..	2	..	..	..	..	..	..	..	..	6	..	1	..	..	..	..	..	..
	2	..	..	..	..	..	..	..	..	..	..	3	..	..	..	..	..	..	..	..	..	..	2	5	..	..	..	1	2
	3	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	3	1	4	5	2	..	2	..	3	..
	4	..	..	..	..	..	..	..	..	..	..	1	..	1	1	3	3	..	..	1	5	1	3	2	5	1	4	..	..
	5	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
	6	..	..	..	..	..	..	..	..	..	..	1	..	..	..	..	..	..	..	..	2	2	..	2	..	..	..	..	..
	7	..	..	..	..	..	..	..	..	..	..	1	..	..	..	..	..	..	..	..	2	..	..	..	2	..	..	..	..
	8	..	..	..	..	..	..	..	..	..	..	1	2	..	..	..	..	..	..	..	1	..	5	2	2	..	1	12	..
	9	..	..	..	..	..	..	..	..	..	..	1	5	..	..	..	..	..	..	..	3	..	..	4	..	..	..	..	..
	10	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1	8	1	..	..	..	1	..
Malnutrition	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
	2	..	..	..	..	..	..	..	..	..	..	..	..	5	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..++
	3	..	..	..	..	..	..	..	..	2	..	4	4	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
	4	..	..	..	..	..	..	..	..	..	..	..	..	5	..	..	..	..	..	1	..	..	..	..	..	..	..	..	..
	6	..	3	..	..	..	2	..	5	..	2	..	..	..	1	..	..	..	4	10	..	..	..	..	..	..	..	..	..
	7	..	..	..	3	..	..	..	..	..	..	..	..	..	..	2	..	..	..	..	..	..	..	..	..	..	..	..	..
	8	..	..	..	..	..	..	..	..	..	..	..	2	..	..	..	2	..	..	..	..	..	..	..	..	..	..	..	..
	9	7	..	..	..	3	4	5	..	1	4	4	3	3	..	..	..	..	..	..	8	..	5	..	..	+++	..	..	..
	10	..	..	..	3	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..

Period of exercise, October 26 to November 21. Period of malnutrition, October 24 to November 5–10. + indicates that right eye was almost closed; ++, died, and +++, inflamed eyelid.

is supposed to be due to an infection involving the labyrinth.) In the malnourished group, all but rat 6 showed marked degrees of restlessness. Blinking of the eyelids was more pronounced in the malnourished rats than in the controls. The number of blinks for fifteen seconds are recorded in table 3. Rat 2 was the only rat of the normal series that

blinked consistently day after day. Of the malnourished rats, on the other hand, seven blinked more or less throughout the entire experiment. This phenomenon cannot be explained either on the basis of conditioning or as the result of local physical irritation. Furthermore, blinking and restlessness began to disappear shortly after an adequate diet was administered.

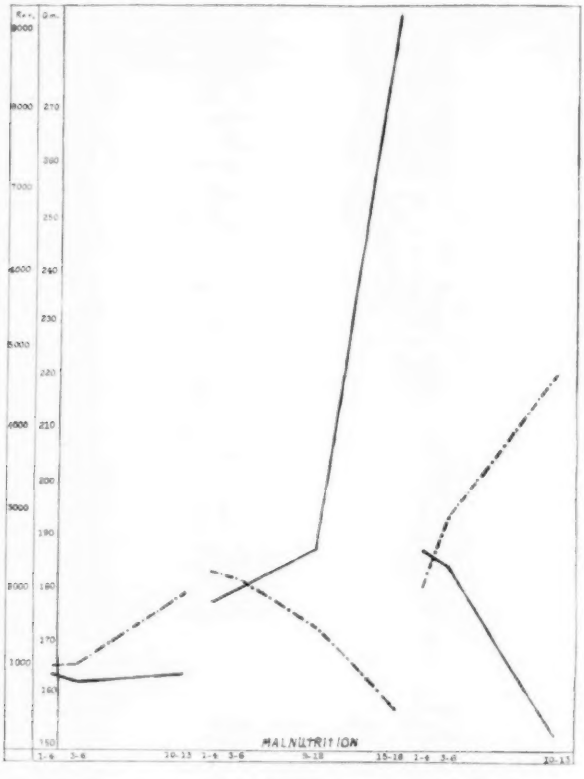


Figure 20

NERVOUSNESS AND FATIGUE IN UNDERNOURISHED CHILDREN

The evidence presented by the experimental study led to the investigation into the symptoms of nervousness and fatigue in malnourished children. Questionnaires (of which copies are included) pertaining to efficiency and habits of living, were submitted to the child, the parent and the teacher. Questions referring to nervousness and fatigue are marked with *N* and *F*, respectively.

Figure 26 represents a study of the health habits and efficiency of 100 normal children and 100 malnourished children, of the same ages.

A glance at the figure shows the marked contrast in both health habits and symptoms of efficiency between the former and the latter.

(*a*) Abnormal children have poorer health habits than normal children (9.6 against 5.65).

(*b*) Their efficiency is almost one third of that of normal children (9.9 against 3.62).

TABLE 4 *A.—Data from Questionnaire to Be Answered by Child*

Per Cent Underweight	Number of Symptoms of Fatigue	Nervousness	Number of Cases
1 - 6	1	2	10
7 - 10	1	2	26
11 - 14	3	4.5	11
15 - 24	2.5	3	5
1 - 9	..	1	27
10 - 14	3	4	16

TABLE 4 *B.—Data from Questionnaire to Be Answered by Mother*

Per Cent Underweight	Number of Symptoms of Fatigue	Nervousness	Number of Cases
1 - 6	..	2	10
7 - 10	..	2	13
11 - 14	3	6.5	15
15 - 24	2	6	10
1 - 9	0.5	2.5	16
10 - 14	3	6	19

TABLE 4 *C.—Data from Questionnaire to Be Answered by Teacher*

Per Cent Underweight	Number of Symptoms of Fatigue	Nervousness	Number of Cases
1 - 6	2	4	10
7 - 10	2	3	23
11 - 14	3	2.5	11
15 - 24	3	6	5
1 - 9	2	4	15
10 - 14	1	3	16

(*c*) The figures 2.4 and 0.53, respectively, indicate that their family history is more positive.

(*d*) Their efficiency, judged by the mother, is worse than that of normal children (8.43 against 4.19).

(*e*) Their efficiency as observed by the teacher is inferior to that of normal children (17.48 as against 8.57).

In tables 4 *A*, 4 *B* and 4 *C*, the analysis of the questionnaires as they pertain to fatigue and nervousness is presented. In the first column is listed the percentage of underweight; in the second, the number of symptoms expressed by the midamount of positive answers to questions

Fig. 21.—Questionnaire of health habits for the child to be answered by the child; page 1.

NAME..... AGE .....SCHOOL.....

ADDRESS..... TEL. .....GRADE.....

QUESTIONNAIRE OF HEALTH HABITS FOR THE CHILD
(TO BE ANSWERED BY THE CHILD)

(1) What time do you go to bed?.....
(2) How long does it take you to fall asleep?.....
(3) What time do you get up in the morning?.....
(4) Do you often wake up during the night?.....
(5) How many sleep in the same room with you?.....
(6) Does anybody sleep in the same bed with you?.....
(7) Do you sleep with your window open?.....
(8) What time do you eat breakfast?.....
(9) How long does it take you to eat breakfast?.....
(10) What do you eat for breakfast? Mention the last three breakfasts you ate.....
(1).....
(2).....
(3).....
(11) What time do you eat lunch?.....
(12) How long does it take you for luncheon?.....
(13) Do you eat luncheon at home or at school?.....
(14) What do you eat for luncheon? Mention the last three luncheons you ate.....
(1).....
(2).....
(3).....
(15) What time do you eat supper?.....
(16) How long does it take you for supper?.....

Fig. 21, page 2.

(17) What do you eat for supper? Mention the last three suppers you ate.....
(1).....
(1).....
(3).....
(18) What green vegetables do you eat? Mention each separately.....
(2).....
(2).....
(3).....
(4).....
(5).....
(6).....
(7).....
(19) How many pieces of candy do you eat a day?.....
(20) When do you eat candy?.....
(21) How many cups of coffee do you drink daily?.....
(22) How many glasses of milk do you drink daily?.....
(23) How often do you use medicines for your bowels?.....
(24) Do you ever take any rests or naps in the daytime?.....
(25) How many hours a day do you spend in out of door play?.....
(26) When do you play out of doors?.....
(27) How many hours do you play indoors?.....
(28) When do you play indoors?.....
(29) How many hours do you spend in home study?.....
(30) When do you do your home study?.....
(31) Name the clubs you belong to.....
(1).....
(2).....
(3).....
(32) How many times a week do you meet with your club?.....

Fig. 21, page 3.

(33) What time of day do you meet with your club?.....
(34) How many times a week do you meet with your band or chorus?.....
(35) What time of day do you meet with your band or chorus?.....
(36) How much time do you practice on your musical instrument?.....
(37) At what time of day do you practice on your instrument?.....
(38) What days of the week do you go to the movies?.....
(39) What time of day do you go to the movies?.....
(40) How often do you listen to the radio?.....
(41) What time of day do you listen to the radio?.....
(42) How many hours a day do you listen to the radio?.....
(43) How many blocks do you live from school?.....
(44) Do you walk to and from school?.....
(45) What chores do you do at home?.....
.....
(46) How long does it take you daily to do these chores?.....
(47) What time of day do you do chores?.....
(48) What do you do after school? .....
(49) What do you do after supper? .....
.....
(50) What do you do before breakfast?.....
(51) What work do you do for pay?.....
(52) How long does this work take you?.....
(53) How much do you earn a week?.....
(54) How many parties in the evening do you go to in a month?.....
(55) What time of the week do you go to parties?.....
(56) How long do you stay at the party?.....
(57) How many dancing lessons a week do you take?.....
(58) When are your dancing lessons?.....
(59) How long does each dancing lesson last?.....
(60) How many books do you read a week?.....

Fig. 22.—Questionnaire of health habits for the child to be answered by the mother; page 1.

NAME..... AGE .....SCHOOL.....
ADDRESS..... TEL. .....GRADE.....

QUESTIONNAIRE OF HEALTH HABITS FOR THE CHILD
(TO BE ANSWERED BY THE MOTHER)

(1) What time does your child go to bed?.....
(2) How long does it take him to fall asleep?.....
(3) What time does he get up in the morning?.....
(4) Does he often wake up during the night?.....
(5) How many sleep in the same room with him?.....
(6) Does anybody sleep in the same bed with him?.....
(7) Does he sleep with his window open?.....
(8) What time does he eat breakfast?.....
(9) How long does it take him to eat breakfast?.....
(10) What does he eat for breakfast? Mention the last three breakfasts he ate.....
(1).....
(2).....
(3).....
(11) What time does he eat lunch?.....
(12) How long does it take him for luncheon?.....
(13) Does he eat luncheon at home or at school?.....
(14) What does he eat for luncheon? Mention the last three luncheons he ate.....
(1).....
(2).....
(3).....
(15) What time does he eat supper?.....
(16) How long does it take him for supper?.....

Fig. 22, page 2.

(17) What does he eat for supper? Mention the last three suppers he ate.....
(1).....
(2).....
(3).....
(18) What green vegetables does he eat? Mention each separately.....
(1).....
(2).....
(3).....
(4).....
(5).....
(6).....
(7).....
(19) How many pieces of candy does he eat a day?.....
(20) When does he eat candy?.....
(21) How many cups of coffee does he drink daily?.....
(22) How many glasses of milk does he drink daily?.....
(23) How often does he use medicines for his bowels?.....
(24) Does he ever take any rests or naps in the daytime?.....
(25) How many hours a day does he spend in out of door play?.....
(26) When does he play out of doors?.....
(27) How many hours does he play indoors?.....
(28) When does he play indoors?.....
(29) How many hours does he spend in home study?.....
(30) When does he do his home study?.....
(31) Name the clubs he belongs to.....
(1).....
(2).....
(3).....
(32) How many times a week does he meet with his club?.....

Fig. 22, page 3.

(33) What time of day does he meet with his club?.....
(34) How many times a week does he meet with his band or chorus?.....
(35) What time of day does he meet with his band or chorus?.....
(36) How much time does he practice on his musical instrument?.....
(37) At what time of day does he practice on his instrument?.....
(38) What days of the week does he go to the movies?.....
(39) What time of the day does he go to the movies?.....
(40) How often does he listen to the radio?.....
(41) What time of the day does he listen to the radio?.....
(42) How many hours a day does he listen to the radio?.....
(43) How many blocks does he live from school?.....
(44) Does he walk to and from school?.....
(45) What chores does he do at home?.....
.....
(46) How long does it take him daily to do these chores?.....
(47) What time of day does he do chores?.....
(48) What does he do after school?.....
(49) What does he do after supper?.....
.....
(50) What does he do before breakfast?.....
(51) What does he do for pay?.....
(52) How long does this work take him?.....
(53) How much does he earn a week?.....
(54) How many evening parties does he go to a month?.....
(55) What time of the week does he go to parties?.....
(56) How long does he stay at the party?.....
(57) How many dancing lessons a week does he take?.....
(58) When are his dancing lessons?.....
(59) How long does each dancing lesson last?.....
(60) How many books does he read a week?.....

Fig. 23.—Questionnaire of efficiency of the child to be answered by the child; page 1.

NAME..... AGE .....SCHOOL.....

ADDRESS..... TEL. .....GRADE.....

QUESTIONNAIRE OF "EFFICIENCY OF THE CHILD"
(TO BE ANSWERED BY THE CHILD)

(1) Do you have headaches every day?.....
(2) Do you have headaches twice a week?.....
(3) Do you have headaches once a week?.....
(4) How many minutes or hours does your headache last?.....
(5) At what time of day does your headache come on?.....
(6) Do you get a headache after reading?.....
(7) Do you get a headache after play?.....
(8) Do you have a backache twice a week?.....
(9) When does your backache come on?.....
(10) Do you have a pain in your arms every day?.....
(11) When do you have a pain in your arms?.....
(12) Do you have a pain in your legs every day?.....
(13) When do you have pain in your legs?.....
(14) Do you ever feel a burning in the muscles?.....
(15) When do you feel a burning in the muscles?.....
(16) Do any of your muscles ache when you are sitting at your school desk?.....
(17) How often do your muscles ache when you are sitting at the school desk?.....
(18) Do your desk and seat hurt you?.....
(19) When do your desk and seat hurt you?.....
(20) Is your desk too high for you?.....
(21) Is your desk too low for you?.....
(22) Do your feet touch the floor when you are sitting at the desk?.....
(23) Do you feel cramped in your seat?.....
(24) When you recite in school, do you stand straight without leaning against the back of your seat?.....
(25) Can you read the writing on the board from where you sit?.....

Fig. 23, page 2.

(26) Do your eyes hurt you during reading in school?.....
(27) Do you have to hold your book close to your eyes when you read?.....
(28) Can you hear the teacher from where you sit?.....
(29) Can you easily hear the other children from where you sit?.....
F (30) Do you feel sleepy in school?.....
F (31) When do you get sleepy in school?.....
F (32) Do you get tired in school easily?.....
(33) When do you get tired in school?.....
F (34) Do you get so tired standing that you would like to sit down?.....
F (35) Do you get tired when playing?.....
(36) Do you get hot in school?.....
(37) When do you get hot in school?.....
(38) Do you feel tired at noon?.....
(39) Do you feel tired after luncheon?.....
(40) Why do you feel tired after luncheon?.....
F (41) Do you feel tired after school is out?.....
(42) Do you feel very tired in the evening before going to bed?.....
F (43) Is it hard for you to get up in the morning?.....
(44) Why is it hard for you to get up in the morning?.....
F (45) Do you feel sort of tired a great deal of that time?.....
(46) What time of day do you feel most tired?.....
(47) Do you usually sleep well?.....
(48) Do you have nightmares?.....
(49) How often do you wake up in the night?.....
(50) Is your appetite good?.....
(51) Is there any kind of food that makes you sick to your stomach?.....
(52) What foods make you sick to your stomach?.....
(53) Do you get sick to your stomach every day?.....
(54) Do you get sick to your stomach twice a week?.....
(55) Do you get sick to your stomach once a week?.....
N (56) Can you sit still without moving around all the time?.....

Fig. 23, page 3.

N (57) Do you play with the things on your desk a great deal?
N (58) Do you bite your finger nails?
N (59) Do you bite your lips?
N (60) Do you suck your thumb?
N (61) Do you pick your nose?
N (62) Do you pick your face?
N (63) Do you put your fingers through your hair a great deal?
(64) Do you have trouble in catching your breath?
(65) When do you have trouble in catching your breath?
(66) Do you get out of breath quickly?
(67) When do you get out of breath?
(68) Does your heart pound so you can hear it?
(69) When does your heart pound so that you can hear it?
(70) How often have you fainted away?
(71) How old were you when you fainted away?
(72) Why did you faint away?
(73) Do you get dizzy often?
(74) When do you get dizzy?
(75) Do things ever get misty before your eyes?
(76) When do things get misty before your eyes?
(77) Do you always feel strong and well?
(78) Why don't you feel strong and well?
(79) Do you feel all in?
(80) Are you worried about your health?
(81) Are you happy most of the time?
(82) Why are you not happy?
(83) Are your feelings often hurt so badly that you cry?
(84) What hurts your feelings so that you cry?
N (85) Do you often get cross over little things?
(86) What makes you cross?
N (87) Do you giggle a great deal and find that you cannot help it?

Fig. 23, page 4.

(88) Do you think that you are easily excited?
(89) What excites you easily?
(90) Do you make friends easily?
(91) Do you keep your friends long?
(92) Do you find school a hard place to get along in?
(93) Why do you find school a hard place to get along in?
(94) Are you anxious to get away from school?
(95) Why are you anxious to get away from school?
(96) Do you like your teachers?
(97) Do you like gymnasium?
(98) Why don't you like gymnasium?
(99) Do you get tired in gymnasium so that you would like to stop before it is over?
(100) Is it hard for you to pay attention to the work in school?
(101) Do you think often of other things than what the teacher wants you to?
(102) Is it hard for you to learn?
(103) Is it hard for you to remember things?
(104) Do you finish what you start out to do?
(105) What don't you finish what you start out to do?
(106) Do you like to play a musical instrument?
(107) Do you like to practice on your instrument?
(108) Do you like going to school mornings?
(109) Do you like going to school afternoons?
(110) Would you like school to be over at noon?
(111) Why would you like school to be over at noon?
(112) What would you do in the afternoon if there was no school?
(113) Would you like to have more recesses?
(114) At what time would you like to have recesses?
(115) What would you prefer to do during these recesses?
(116) What lessons would you like best in the morning?
(117) What lessons would you like best in the afternoon?

Fig. 24.—Questionnaire of efficiency of the child to be answered by the teacher; page 1.

NAME..... AGE .....SCHOOL.....

ADDRESS..... TEL. .....GRADE.....

QUESTIONNAIRE OF "EFFICIENCY OF THE CHILD"

(TO BE ANSWERED BY THE TEACHER)

(1) Does this child seem happy, indifferent, or unhappy?.....
N (2) Does he appear dejected, sullen, anxious, tense?.....
N (3) Has he any speech defect?.....
N (4) Has he had any speech defect?.....
N (5) Is he reliable or unreliable?.....
(6) Is he accurate or inaccurate?.....
(7) Does he concentrate well, fair or poorly?.....
(8) Does he show great, average, or slight interest in his work?.....
(9) Is he what you would call a good worker?.....
(10) Does he finish what he starts out to do?.....
(11) Is he slow or fast in his movements?.....
(12) Does he work hard or lazily?.....
(13) Does he play hard or lazily?.....
(14) Is he clumsy or awkward?.....
N (15) Is he overactive, active, or lazy?.....
(16) Does he see well?.....
(17) Does he hear well?.....
(18) Does he idle away his time?.....
F (19) Can he stand a lot or does he tire quickly?.....
F (20) Would you consider him a delicate child?.....
F (21) Would you say he lacked strength?.....

Fig. 24, page 2.

(22) Does he look pinched and tired?.....
(23) Has he dark circles around his eyes?.....
N (24) Would you consider him a nervous child?.....
(25) Is he irritable, quiet, or listless?.....
N (26) Does he sit quietly in his chair without moving around all the time?.....
N (27) Does he suck his thumb?.....Bite his fingernails?.....Bite his lips?..... Pick his nose?.....Put his fingers through his hair?.....Pick his face? .....
N (28) Is he easily excited?.....
N (29) Is he boisterous and talkative?.....
N (30) Does he giggle a great deal?.....
N (31) Is he hard to manage?.....
(32) Does he make friends easily?.....
(33) Does he keep his friends long?.....
(34) What grades has he skipped?.....
(35) What grades has he repeated?.....
(36) Does he come to school on time?.....
(37) How many days per month does he miss on account of sickness?.....
(38) How many days per month does he miss for any other cause?.....
F (39) Does he feel sort of tired a great deal of the time?.....
F (40) Does he complain a great deal of being tired?.....
(41) Does he compain of headaches?.....Backaches?.....Muscle pain?..... Eyeache?.....Burning in muscles?.....Dizziness?.....Feelings of Fainting?.....Pounding of heart?.....
(42) Does he complain of not feeling well?.....
F (43) Does he complain of feeling sleepy in school?.....
(44) Does he complain that gymnasium tires him?.....

Fig. 24, page 3.

(45) Does he look sleepy?.....At what time of day?.....
F (46) Does he ever fall asleep while in class?.....
F (47) Does he put his head on the desk to sleep?.....
(48) Does he rest his head in his hands?.....
N (49) Does he chew gum or candy in class?.....
N (50) Does he pucker his lips or frown during work?.....
N (51) Does he chew his pencil or pen?.....Play with something when in his seat? .....
(52) Does he look out of the window a great deal?.....
(53) Does he look over the desks of other children a great deal?.....
(54) Does he usually lean on something when he stands?.....
N (55) Does he blink?....Twist his hands?....Crack his knuckles a great deal?....
(56) Does he whisper to his classmates?.....
(57) Does he whisper to his classmates?.....
(58) Does he stand upright on both feet when he recites?.....
F (59) Does he sigh or yawn a great deal?.....
(60) Is his posture good or poor when standing?.....When sitting?.....
N (61) Has he good control over his actions?.....
(62) We shall appreciate any further information you can give us regarding this child .....
.....
.....
.....
.....
.....

Fig. 25.—Questionnaire of efficiency of the child to be answered by the mother; page 1.

NAME..... AGE .....SCHOOL.....
ADDRESS..... TEL. .....GRADE.....

QUESTIONNAIRE OF "EFFICIENCY OF THE CHILD"
(TO BE ANSWERED BY THE MOTHER)

(1) Does your child seem happy, indifferent or unhappy?.....
N (2) Does he appear dejected, sullen, anxious, tense?.....
N (3) Has he any speech defect?.....
N (4) Has he had any speech defect?.....
N (5) Is he reliable or unreliable?.....
N (6) Is he accurate or inaccurate?.....
(7) Does he concentrate well, fairly, poorly?.....
(8) Does he show great, average, or slight interest in his work?.....
(9) Is he what you would call a good worker?.....
(10) Does he finish what he starts out to do?.....
(11) Is he slow or fast in his movements?.....
(12) Does he work hard or lazily?.....
(13) Does he play hard or lazily?.....
(14) Is he clumsy or awkward?.....
N (15) Is he overactive, active or lazy?.....
(16) Does he see well?.....
(17) Does he hear well?.....
(18) Does he idle away his time?.....
F (19) Can he stand a lot, or does he tire quickly?.....
(20) Would you consider him a delicate child?.....
F (21) Would you say he lacks strength?.....
F (22) Does he look pinched and tired?.....
(23) Has he dark circles around his eyes?.....
N (24) Would you consider him a nervous child?.....

Fig. 25, page 2.

N (25) Is he irritable, quiet, or listless?.....
N (27) Does he sit quietly in his chair without moving around all the time?.....
N (28) Does he suck his thumb?..... Bite his finger nails?..... Bite his lips?..... Pick his nose?..... Put his fingers through his hair? Pick his face?.....
N (29) Is he easily excited?.....
N (30) Is he boisterous and talkative?.....
N (31) Does he giggle a great deal?.....
N (32) Is he hard to manage?.....
(33) Does he make friends easily?.....
(34) Does he keep his friends long?.....
(35) What grades has he skipped?.....
(36) What grades has he repeated?.....
(37) Does he come to school on time?.....
(38) How many days per month does he miss on account of sickness?.....
(39) How many days per months does he miss for any other cause?.....
F (40) Does he feel sort of tired a great deal of the time?.....
F (41) Does he complain a great deal of being tired?.....
(42) Does he complain of headaches?..... Backaches?..... Muscle pain?..... Eyeache?..... Burning in muscles?..... Dizziness?..... Feelings of fainting?..... Pounding of the heart?.....
(43) Does he complain of not feeling well?.....
(44) Does he complain of feeling sleepy in school?.....
(45) Does he complain that gymnasium tires him?.....
F (46) Is it hard for him to get up in the morning?.....
(47) Does he sleep well?.....
(48) Has he nightmares?.....
(49) Does he wet his bed?.....
(50) How often does he wake up at night?.....

Fig. 25, page 3.

(51) Is his appetite good?.....
(52) What kind of food makes him sick to his stomach?.....
(53) Does he get out of breath quickly?..... When?.....
(54) Has he ever fainted away?..... When?.....
(55) Does he get dizzy often?..... When?.....
56) Does he like to go to school?.....
F (57) Does he ever come in from play and lie down?.....
(58) Does he run and play and fight as other children do?.....
(59) Or does he prefer to stay indoors?.....
F (60) Does he get out of breath during play more easily than other children?.....
(61) Who else in the family is always tired? .....
(62) Who else in the family is known as a delicate person?.....
.....
(63) Who else in the family is underweight? .....
(64) Who else in the family is nervous?.....
(65) Who on either side of the parents has or has had the following diseases? Consumption..... Heart disease..... Blood disease..... Cancer..... Kidney trouble..... Goiter..... Diabetes..... Nervous and mental diseases..... Periodic headaches..... Paralysis..... Stroke..... St. Vitus dance..... Epilepsy..... Convulsions..... Fainting spells..... Insanity .....
(66) How old were you when you gave birth to your child?.....
(67) Is he an only child?.....
(68) How much did he weigh at birth?.....
(69) Did you have trouble in feeding him?.....
(70) Was he restless as a baby?.....
(71) Did he cry a great deal?.....
(72) What severe illness has he had?.....
(73) Tell diseases and ages.....

relative to fatigue; in the third, the number of symptoms referring to nervousness, and in the last the number of cases studied.

One can see at a glance that in children more than 100 per cent underweight, the frequency of symptoms both of fatigue and of nervousness is higher than in children with a weight-height idex within 10 per cent of the normal. Thus the clinical observations bear out the evidence presented by experimental work that poor nutrition is associated with excessive activity.

THERAPEUTICS

The experimental study of the effects of undernutrition on the activity of rats and the clinical observations in undernourished children suggest a procedure of treatment which has as its basis the "forced-feeding-rest cure."

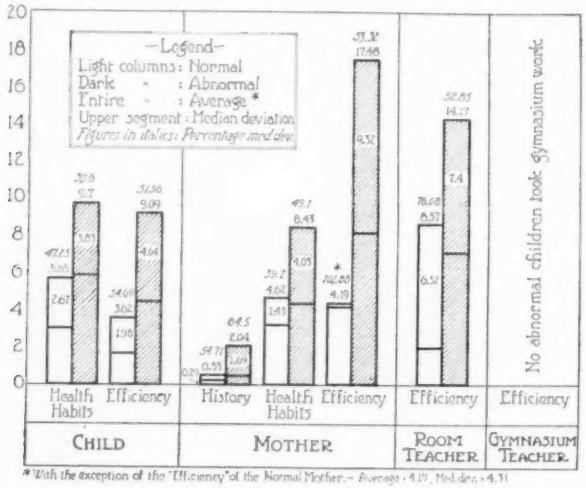


Fig. 26.—Comparison of questionnaires of normal and abnormal subjects.

In 1891, Weir Mitchell [8] published his famous monograph "Fat and Blood" in which he proposed a so-called rest-forced-diet cure for certain cases of nervous exhaustion. By enforced rest in bed and frequent feedings (seven to eight times a day) he succeeded in improving and oftentimes even curing patients who for many years had been suffering from symptoms of neurasthenia. He is one of the first American clinicians who showed by the trial and error method that diets deficient qualitatively and quantitatively will produce functional disorders of the nervous systems. It has been proved, without a question of doubt, that insufficient amounts of vitamin C, found chiefly in fresh fruits, will cause

8. Mitchell, Weir: Fat and Blood, Philadelphia, J. B. Lippincott Company 1891.

scurvy which, in its mild form, is characterized by listlessness, irritability and a decrease in general functional capacity; in its more severe forms by weakness, dyspnea, convulsions and delirium. Again, in beriberi, which is probably due to a deficiency in the diet of vitamin B and to an excess of carbohydrates, one finds a neuritis affecting the motor and sensory nerves, general weakness and depression of function, numbness and stiffness of the legs and edema of the ankles. Also in pellagra, chiefly the nervous system becomes involved. In 1914, Goldberger [9] found that the children in a children's home were suffering from pellagra, while nurses and attendants remained immune. On investigation, he noticed that the diet of the former was meager in fresh proteins. Their condition was soon cured when liberal amounts of fresh meat, eggs, milk and green vegetables were added to the dietary.

He then artificially produced this disease in man by administering the diet used by persons with pellagra.

Again, Voegtlin,[10] in 1920, treated successfully patients suffering from pellagra by making prominent in their diet milk, prunes, orange juice, meat, eggs and butter.

These are only a few of the many facts which show clearly that even mild transgressions in diet or the omission of just one food element may seriously affect mental and physical health. Modern pediatricians have in the past centered their attention on infant feeding; yet they have neglected the details of the feeding of school children. Few references on this subject can be found in pediatric literature. Cramer [11] suggested that many so-called "repeaters" in school may have undiagnosed cases of malnutrition and that many borderline cases of malnutrition in children have been neglected or undiagnosed. Lowered vitality, retarded growth and inferior mental efficiency may often be due to a lack of food rich in vitamins. This may account for the fact that about one third of the American school children are malnourished and another third potential victims of malnourishment.

Attention, therefore, must be given not only to the quantity of food, but also to its quality. We often are not aware of the qualitative inadequacy of average diets of some races. Indigestible foods, foods lacking in certain essential elements, racial customs of cooking, all have a bearing on nutritional processes. McCollum was the first to emphasize the importance of the biologic value of all the food elements in relation to each other. He writes:

---

9. Goldberger, J.: The Transmissibility of Pellagra, Pub. Health Rep., 1916, vol. 31.

10. Voegtlin, C.: Recent Work on Pellegra, Harvey Lecture Series, 1919-1920.

11. Cramer, W.: Vitamin Underfeeding, Brit. J. Eper. Path. **3**:298, 1922; Vitamins and the Borderland Between Health and Disease, Lancet **1**:633, 1924.

We have reached the conclusion that it is not possible to state the amount of any food factor which constitutes the minimum or the optimum, or an excess, without taking into consideration the biological values of each of the other factors in the diet. The minimum amount of any dietary factor of constant quality which will just serve to maintain apparently normal well-being, will fail to suffice when another factor is modified so as to be unsatisfactory, and after such a modification of the diet increasing either of the two factors under consideration will suffice to protect the body from harm in some measure. There is a principle of relativity which is of fundamental importance in estimating the value of a diet as a whole. The diet must be considered as made up of a number of factors, and an effort made to adjust each factor at the optimum.

It can be said in general that the diet of the average American child is too rich in sugar, confectioneries and sweet beverages, and too meager in protective foods such as milk, leafy vegetables and fresh fruits. Foods that can be served quickly, such as canned goods and smoked meats, are the favorites of the modern housewife. The American dietary is, therefore, inclined to be especially deficient in calcium, in vitamin A and also somewhat in vitamin C.

One cannot write on the subject of dietary without saying at least a few words on the importance of a proper psychologic background for eating, namely, palatability, color, texture and temperature of foods. All these factors influence digestion and assimilation. So do emotions such as grief, anger, worry, irritation, emotional and physical strain. According to Cannon, Pavlow and Carlson the emotions may cause physiologic changes in the gastro-intestinal tract, which, in turn, may bring on a loss in weight.

The second therapeutic measure, namely, rest and relaxation, has not been used sufficiently in malnutrition, though it must be viewed as nature's chief ally. Rest, in its correct form, slows down general metabolism and decreases functional activity. When a person is lying down, the pulse rate as well as the rate of respiration becomes considerably slower. Next to sleep, rest is the best antidote to fatigue from which many malnourished children suffer. In malnutrition, the general efficiency is usually reduced. Thus the output of energy is in inverse proportion to achievement. This fact makes rest all the more imperative. It is therefore not surprising to find recovery much hastened in children who have been taken out of school and put to bed for from seven to ten days. Psychologically speaking, it is easier to get a child to stay in bed a whole day than to have him take an hour rest period. Furthermore, the relief from stimulation and irritation of a long school day of mental and emotional work has a beneficial effect on the overwrought nervous system of the malnourished child.

Relaxation has also been shown to have a definite physiologic effect on the nervous system. Malnourished children usually do not know how to relax. In spite of their emaciation, they are often muscle-

bound. Applying Jacobson's [12] technic, it is not difficult to teach them the art of relaxation. In a quiet room, the attendant or nurse instructs the child in a quiet voice how to relax. Lying on his back in bed, with his mouth slightly open and his eyes closed, the child holds the arms stretched out at about 45 degrees to the body and attempts to make them "as limp as a rag." Relaxation is then extended to the legs which are held out at about the same angle. With the muscles of the arms, the trunk and the legs relaxed, the child remains in this position for thirty minutes. The procedure is repeated four times a day during the rest cure. When the child is allowed to be up and around again, the number of relaxation periods are reduced to two. With persistent effort, practically every child will finally acquire the habit of proper relaxation.

REPORTS OF CASES

Three cases are discussed in full to show the improvement following forced-feeding-rest cure.

CASE 1.—H. L., a boy, aged 12, had been termed by psychiatrists and psychologists a "nervous hyperkinetic child." He was unusually high strung, restless and excitable. To use his own words, "I have to keep on going and be doing something." His motor control was deficient. He cracked his knuckles, bit his fingernails, made grimaces, and finally began to stutter and stammer. The tonsils had been removed. He was normal in weight (height-weight index 2 per cent below normal). The muscle tone was good. In fact, he seemed well developed and well nourished for his age.

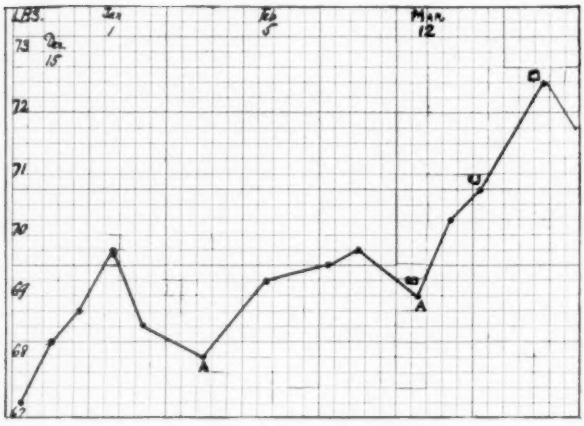
In looking over his answers to the questionnaire, it was found that his food intake had been limited to about two thirds of his caloric needs. His diet was meager in meats and vegetables and rich in candy and cookies. This inadequacy of diet allied with hyperkinesis suggested the treatment of forced feeding in bed. The diet sheet is shown subsequently below.

Diet for Forced Feeding in Case 1

		Calories
7 a. m.	Oatmeal, 10 tablespoonfuls	250
	Bread, 2 slices	200
	Butter, 1 pat	100
	Baked apple	100
	Milk, 1 glass	160
	Cream, 3 ounces	160
	Total	970
10 a. m.	Milk, 1 glass	160
	Cookies, arrow root, 2	50
	Fig, 1 small	50
	Total	260

12. Jacobson, A.: J. Nerv. & Ment. Dis. **45:** 464, 1920.

1 p. m.	Roast lamb, 4 oz.	200
	Baked potato	150
	Bread, 2 slices	200
	Butter, 1 pat	100
	Peas, 4 tablespoonfuls	100
	Rice pudding, 2 tablespoonfuls	100
	Milk, 1 glass	160
	Total	1,010
4 p. m.	Orange	100
	Crackers, 2 graham	100
	Total	200
6:30 p. m.	Egg, 1 scrambled	150
	Bread, 2 slices	200
	Butter, 1 pat	100
	Milk, 1 glass	160
	Total	610



27.—Weight curve of a malnourished child treated with forced feeding and rest cure. *A* indicates when child was ill; *B*, half day session — in bed for the rest of the day; *C*, half day session, bed week ends, and *D*, full day school following refusal to cooperate.

The total calories value of this sample menu is 3,050 against from 2,500 to 2,700 calories usually administered to children 12 years of age.

The child gained 2 pounds (0.9 Kg.) in eight days. After ten days his stuttering and stammering disappeared. He slept better and his restlessness decreased. He was then allowed to return to school with one hour rest in the afternoon and with all day Saturday and Sunday in bed. His out-of-door play time was restricted to one hour. Four feedings amounting to 2,500 calories were substituted for the previous five feedings of about 3,000 calories. He has been on

this schedule of rest and feeding now for one month. His parents, his nurse, his teachers all are agreed that his general condition, especially his motor control has markedly improved.

CASE 2.—A. C., a girl, aged 13, was 16 per cent underweight. The diagnosis was malnutrition, fatigue and nervousness. A summary of her health habits and her efficiency is given subsequently. The same treatment was instituted as in case 1 except that on account of being older more food was given. After ten days in bed, nausea and nervous exhaustion disappeared, and her general nervousness was less marked. She gained 2 pounds (0.9 Kg.) in weight during that period. She was then allowed to return to school, with the understanding that she was to take a nap after school. Week ends and holidays were also spent in bed. The latter instructions were omitted after four weeks. During the following seven months she increased her weight by 18 pounds (8.2 Kg.). Today her muscle tone is good; she has excellent color, and her functional capacity is practically that of a normal child.

CASE 3.—E. N., a girl, aged 12, had a weight-height index of 17 per cent below normal. A summary of her efficiency and health habits is given subsequently. The weight curve (fig. 27) needs explanation.

At first the usual method of treatment was instituted: that is, bad food habits were corrected, and the amount of sleep was increased to eleven and one-half hours. During four months, her weight increased only from 67¼ pounds to 69 pounds (30.5 to 31.3 Kg.). She was therefore allowed to attend school only mornings and to spend the afternoons in bed resting and relaxing. She was given food five times a day at three hour intervals. The following month she gained 3½ pounds (1.6 Kg.) and showed a great improvement in her nervous symptoms.

When, after that time, she refused to cooperate, she was allowed to return to school for both sessions. She lost 1½ pounds (0.7 Kg.) during the following week.

Summary of Health and Efficiency of Child in Case 3

HEALTH HABITS REPORTED BY THE CHILD	EFFICIENCY REPORTED BY THE CHILD
1. Insufficient sleep	1. Headaches in p. m.
2. Insomnia	2. Pain in legs
3. Excess amount of candy	3. Leans on seat when reciting
4. Constipation	4. Sleepy in school at 2:30
5. Movies at night	5. Tires easily in school
6. Shares bed with sister	6. Tires when standing
7. Inadequate luncheon, breakfast, supper	7. Tires after school
8. Candy between meals	8. Most tired in afternoon
	9. Hard to get up in morning
	10. Plays with things on desk
	11. Feels all in
	12. Sensitive
	13. Worries about her health
	14. Easily excited
	15. Anxious to leave school, does not like school
	16. Hard to learn
	17. Hard to remember things

HEALTH HABITS REPORTED BY MOTHER

1. Shares room with two and bed with one
2. Inadequate luncheons and suppers
3. Excessive amount of candy
4. Constipation

EFFICIENCY REPORTED BY MOTHER

1. Concentration fair
2. Lazy worker
3. Looks pinched and tired
4. Nervous
5. Cannot sit still
6. Slow in her movements
7. Does not make friends easily

EFFICIENCY REPORTED BY TEACHER

1. Tires quickly
2. Lacks strength
3. Looks pinched and tired
4. Nervous
5. Excitable
6. Sighs and yawns during lessons

SUMMARY AND CONCLUSIONS

The effect of malnutrition on activity was studied in ten male rats, ten additional rats being kept for control. A clinical study of malnutrition in children with special emphasis on symptoms of nervousness and fatigue and on health habits was carried out. A procedure of treatment of malnourished children is suggested

The experimental work suggests: (1) Hunger is the cause of activity. (2) A positive relation exists between activity and loss in weight. (3) In malnutrition an adequate diet reduces the activity with a simultaneous increase in weight. (4) Inanition produces irritability, restlessness and blinking in rats.

The clinical study of malnourished children suggests that the symptoms of nervousness and fatigue are more numerous in children whose weight-height index is more than 10 per cent below the standard than in children whose weight-height index is less than 10 per cent below the normal.

The forced feeding and rest cure for malnourished children reduces and improves nervous symptoms, increases functional capacity, and hastens the gain in weight.

ASTHMA IN CHILDREN

VIII. A COMPARATIVE STUDY OF THE DIRECT AND INDIRECT (LOCAL PASSIVE TRANSFER) METHODS OF SKIN TESTING WITH THE SCRATCH AND INTRADERMAL TECHNICS *

M. MURRAY PESHKIN, M.D.
AND
A. H. FINEMAN, M.D.
NEW YORK

In the past decade, skin testing (scratch and intradermal) with various substances has come to play an important rôle in the determination of etiologic factors of bronchial asthma and allied conditions. The information derived from testing the patient himself, known as the "direct method" of skin testing, has brought about a rational method of treatment for allergic conditions. However, the testing of infants with asthma, and especially those with dermatoses such as eczema and urticaria, presents many difficulties. Prausnitz and Küstner [1] first demonstrated that when blood serum of a patient sensitive to a protein is injected intradermally into the skin of a normal person, the area in which the injection is made becomes locally sensitized to the specific protein. Local passive transfer of hypersensitiveness into normal human beings was verified by de Besche,[2] Coca and Grove [3] and others. The specific reacting substance in the blood of a person sensitive to a protein was termed "atopic reagin." [3] This method of skin testing is known as the "indirect method." In a study of eleven children, Walzer and Kramer [4] found that the indirect method of testing (intradermal technic) was feasible. They also reported the additional advantage that the danger of a general (constitutional) reaction was eliminated.

The present study in local passive transfer is based on eighteen patients with asthma ranging in age from 7 months to 14 years. Five of these children also have hay-fever, six have or have had eczema and two have urticaria. All of these children were under observation for two years.

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* From the Children's Asthma Clinic, Mount Sinai Hospital.

1. Prausnitz, C., and Küstner, H.: Centralbl. f. Bakteriol. **186**:160, 1921.

2. De Besche, A.: Studies on the Reactions of Asthmatics and on Passive Transference of Hypersusceptibility, Am. J. M. Sc. **166**:265 (Aug.) 1923.

3. Coca, A. F., and Grove, E. F.: Studies in Hypersensitiveness; A Study of the Atopic Reagin, J. Immunol. **10**:445 (March) 1925.

4. Walzer, M., and Kramer, S. D.: Studies in Specific Hypersensitiveness; An Indirect Method of Testing for Conditions of Atopic Hypersensitiveness (A Preliminary Report), J. Immunol. **10**:835 (Sept.) 1925.

TECHNIC OF THE TESTS

Each child was first directly tested by the scratch and intradermal technics with thirty-three different protein substances. The proteins employed for the scratch test were in powdered form. The corresponding fluid extracts employed for the intradermal tests were furnished by Dr. A. F. Coca of the New York Hospital.

After the completion of the direct skin tests, approximately 10 cc. of blood was drawn from the vein of each child and was defibrinated and centrifugalized. The serum thus obtained was passed through a sterile Berkefeld filter. The mother of the child was usually chosen as the subject for the passive transfer tests. Each mother used was first proved to be receptive to passive transfer. The blood serum employed for this purpose was obtained from a patient sensitive to ragweed pollen. One tenth of a cubic centimeter of the undiluted blood serum obtained from the child was injected intradermally in twenty-four sites 1 inch (2.5 cm.) apart on the upper extremities of the subject—six on the volar aspect of each forearm and six on the outer surface of each arm. Sensitization tests were begun within from twenty-four to forty-eight hours. The sensitized sites on the forearms were used for the scratch and those on the arms for the corresponding intradermal tests. For the scratch test the cut was made just over the center of the sensitized area, and for the intradermal test the fluid extract was injected directly into the sensitized site. Each sensitized site was controlled by testing the normal skin 3 or 4 cm. away. A sensitized site which exhibited a positive reaction was not tested again with the same extract or with one biologically related. Tests were usually performed at intervals of two days. All reactions above the control were repeated at some subsequent time for confirmation. When tests were repeated on sites that had been used previously, the size of the first reaction was recorded. However, occasionally it was necessary to make new serum sites, and then an average of the readings was recorded.

The details of the technic of the tests (scratch and intradermal), the type of reactions and their interpretation were described in a recent communication.[5]

The total number of tests performed (exclusive of "repeats" and controls) was 2,352. These tests were begun in May and completed in September, 1926.

The cases will be considered under two groups: those showing sensitization (1) to the inhalant and (2) to the food proteins.

SENSITIZATION TO THE INHALANT PROTEINS

Table 1 shows the comparative results of the scratch and intradermal technics with the direct and indirect methods of skin testing to the common inhalant proteins.

Table 1 shows that many of the positive inhalant reactions obtained by direct test with either the scratch or the intradermal technic were definitely negative by the indirect method. In many of these instances, the positive reactions obtained by direct test were etiologic factors of asthma. The discrepancies between the direct and indirect methods of testing will be better understood by citation of salient facts in some of these cases.

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5. Peshkin, M. M., and Fineman, A. H.: Asthma in Children: VI. A Comparative Study of the Scratch and Intradermal Methods of Skin Testing, Am. J. Dis. Child. **34**:815 (Nov.) 1927.

TABLE 1.—*Corresponding Scratch and Intradermal Reactions to Eighteen Inhalant Substances with the Direct and Indirect (Local Passive Transfer) Methods of Skin Testing*

Skin Reactions	Number of Reactions	Scratch Test: Direct Method —	±	+	++	+++ and ++++	Scratch Test: Indirect Method —	±	+	++	+++	Intradermal Test: Direct Method Negative —	±	+	Positive ++	+++	Intradermal Test: Indirect Method Negative —	±	+	Positive ++	+++
House Dust																					
±.....	3	2	1	0	0	0	0	1	1	1	0	2	0	1	0	0					
+.....	9	8	0	1	0	0	0	0	4	4	1	5	1	2	1	0					
++.....	1	1	0	0	0	0	0	0	1	0	0	1	0	0	0	0					
++++..	1	1	0	0	0	0	0	0	0	1	0	1	0	0	0	0					
Positive.	14	12	1	1	0	0	0	1	6	6	1	9	1	3	1	0					
Negative	4	4	0	0	0	0	0	1	3	0	0	2	0	2	0	0					
Total.	18	16	1	1	0	0	0	2	9	6	1	11	1	5	1	0					
Rabbit Hair																					
±.....	4	4	0	0	0	0	2	0	2	0	0	4	0	0	0	0					
+.....	4	4	0	0	0	0	2	1	0	1	0	4	0	0	0	0					
++++..	2	0	0	0	0	2	0	0	0	1	1	0	0	0	1	1					
Positive.	10	8	0	0	0	2	4	1	2	2	1	8	0	0	1	1					
Negative	8	8	0	0	0	0	7	1	0	0	0	8	0	0	0	0					
Total.	18	16	0	0	0	2	11	2	2	2	1	16	0	0	1	1					
Horse Dander																					
±.....	5	5	0	0	0	0	2	1	2	0	0	5	0	0	0	0					
++.....	3	2	0	0	1	0	0	0	3	0	0	3	0	0	0	0					
++++..	1	1	0	0	0	0	0	0	0	1	0	1	0	0	0	0					
Positive.	9	8	0	0	1	0	2	1	5	1	0	9	0	0	0	0					
Negative	8	8	0	0	0	0	7	1	0	0	0	7	0	1	0	0					
Total.	17	16	0	0	1	0	9	2	5	1	0	16	0	1	0	0					
Ragweed																					
+.....	2	2	0	0	0	0	1	1	0	0	0	2	0	0	0	0					
++.....	1	1	0	0	0	0	0	0	1	0	0	1	0	0	0	0					
Positive.	3	3	0	0	0	0	1	1	1	0	0	3	0	0	0	0					
Negative	15	15	0	0	0	0	12	2	1	0	0	15	0	0	0	0					
Total.	18	18	0	0	0	0	13	3	2	0	0	18	0	0	0	0					
Timothy																					
Positive.	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0					
Negative	18	18	0	0	0	0	17	0	1	0	0	18	0	0	0	0					
Total.	18	18	0	0	0	0	17	0	1	0	0	18	0	0	0	0					
Cat Dander																					
±.....	3	2	0	0	1	0	2	0	0	1	0	2	0	0	1	0					
+.....	1	1	0	0	0	0	0	1	0	0	0	1	0	0	0	0					
Positive.	4	3	0	0	1	0	2	1	0	1	0	3	0	0	1	0					
Negative	14	13	1	0	0	0	13	0	1	0	0	14	0	0	0	0					
Total.	18	16	1	0	1	0	15	1	1	1	0	17	0	0	1	0					
Dog Dander																					
±.....	1	1	0	0	0	0	0	0	1	0	0	1	0	0	0	0					
+.....	1	1	0	0	0	0	1	0	0	0	0	1	0	0	0	0					
Positive.	2	2	0	0	0	0	1	0	1	0	0	2	0	0	0	0					
Negative	16	16	0	0	0	0	12	2	2	0	0	14	1	1	0	0					
Total.	18	18	0	0	0	0	13	2	3	0	0	16	1	1	0	0					
Chicken Feathers																					
±.....	3	2	1	0	0	0	1	2	0	0	0	3	0	0	0	0					
+.....	1	1	0	0	0	0	1	0	0	0	0	1	0	0	0	0					
Positive.	4	3	1	0	0	0	2	2	0	0	0	4	0	0	0	0					
Negative	14	14	0	0	0	0	10	0	4	0	0	13	0	0	1	0					
Total.	18	17	1	0	0	0	12	2	4	0	0	17	0	0	1	0					
Duck Feathers																					
±.....	4	4	0	0	0	0	3	0	1	0	0	3	0	1	0	0					
+.....	1	1	0	0	0	0	0	1	0	0	0	1	0	0	0	0					
++.....	1	1	0	0	0	0	0	0	1	0	0	1	0	0	0	0					
Positive.	6	6	0	0	0	0	3	1	2	0	0	5	0	1	0	0					
Negative	12	12	0	0	0	0	10	2	0	0	0	12	0	0	0	0					
Total.	18	18	0	0	0	0	13	3	2	0	0	17	0	1	0	0					

TABLE 1.—*Corresponding Scratch and Intradermal Reactions to Eighteen Inhalant Substances with the Direct and Indirect (Local Passive Transfer) Methods of Skin Testing—Continued*

Skin Reactions	Number of Reactions	Scratch Test: Direct Method					Scratch Test: Indirect Method					Intradermal Test: Direct Method					Intradermal Test: Indirect Method				
						+++ and ++++					+++ and ++++	Negative			Positive		Negative			Positive	
		—	±	+	++		—	±	+	++		—	±	+	++	+++	—	±	+	++	+++
Goose Feathers																					
±.....	2	1	1	0	0	0	2	0	0	0	0	**2**	0	0	0	**0**					
+.....	1	1	0	0	0	0	1	0	0	0	0	1	0	0	0	0					
++.....	1	1	0	0	0	0	0	0	1	0	0	1	0	0	0	0					
Positive.	4	3	1	0	0	0	3	0	1	0	0	4	0	0	0	0					
Negative	14	14	0	0	0	0	11	3	0	0	0	14	0	0	0	0					
Total.	18	17	1	0	0	0	14	3	1	0	0	18	0	0	0	**0**					
Goat Hair																					
±.....	1	1	0	0	0	0	0	1	0	0	0	1	0	0	0	**0**					
+.....	1	1	0	0	0	0	1	0	0	0	0	1	0	0	0	0					
Positive.	2	2	0	0	0	0	1	1	0	0	0	2	0	0	0	0					
Negative	16	16	0	0	0	0	11	2	**2**	1	0	14	1	1	0	**0**					
Total.	18	18	0	0	0	0	12	3	2	**1**	0	16	1	1	0	**0**					
Orris Root																					
Positive.	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	**0**					
Negative	18	18	0	0	0	0	14	3	1	0	0	17	1	0	0	0					
Total.	18	18	0	0	0	0	14	3	1	0	0	17	1	0	0	0					
Tobacco																					
Positive.	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	**0**					
Negative	15	15	0	0	0	0	7	3	5	0	0	15	0	0	0	0					
Total.	15	15	0	0	0	0	7	3	5	0	0	15	0	0	0	**0**					
Pyrethrum (Insecticide)																					
Positive.	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	**0**					
Negative	18	18	0	0	0	0	9	7	2	0	0	18	0	0	0	0					
Total.	18	18	0	0	0	0	9	7	2	0	0	18	0	0	0	**0**					
Cottonseed																					
±.....	1	1	0	0	0	0	1	0	0	0	0	1	0	0	0	**0**					
+.....	1	1	0	0	0	0	0	1	0	0	0	1	0	0	0	0					
Positive.	2	2	0	0	0	0	1	1	0	0	0	2	0	0	0	0					
Negative	16	16	0	0	0	0	13	3	0	0	0	16	0	0	0	0					
Total.	18	18	0	0	0	0	14	4	0	0	0	18	0	0	0	**0**					
Kapok																					
±.....	1	1	0	0	0	0	0	1	0	0	0	1	0	0	0	0					
+.....	1	1	0	0	0	0	1	0	0	0	0	1	0	0	0	0					
Positive.	2	2	0	0	0	0	1	1	0	0	0	2	0	0	0	0					
Negative	16	16	0	0	0	0	15	1	0	0	0	15	0	1	0	0					
Total.	18	18	0	0	0	0	16	2	0	0	0	17	0	1	0	0					
Le Paige's Glue																					
Positive.	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	**0**					
Negative	17	17	0	0	0	0	16	0	1	0	0	17	0	0	0	0					
Total.	17	17	0	0	0	0	16	0	1	0	0	17	0	0	0	**0**					
Horse Serum *																					
±.....	1	1	0	0	0	0	0	0	1	0	0	1	0	0	0	0					
+.....	1	1	0	0	0	0	0	0	0	0	1	1	0	0	0	0					
Positive.	2	2	0	0	0	0	0	0	1	0	1	2	0	0	0	0					
Negative	16	16	0	0	0	0	11	2	2	1	0	16	0	0	0	0					
Total.	18	18	0	0	0	0	11	2	3	1	1	18	0	0	0	0					

* Included here for convenience.

Two children with asthma and hay-fever each showed a one plus scratch reaction to short ragweed with the direct method and negative reactions with the indirect method. The corresponding intradermal reactions in these two cases were negative with both the direct and the

indirect methods, though the extract used contained a concentration of 0.25 mg. of nitrogen per cubic centimeter. Another child with a negative history of pollen sensitiveness showed a two plus scratch and a one plus intradermal reaction by direct test and negative reactions by indirect test.

It is of interest to note that in three other children with asthma associated with hay-fever all skin tests with ragweed pollen were negative. One of these children who was clinically sensitive to timothy pollen also reacted negatively. All three cases showed positive reactions to pure pollen by the conjunctival test. These observations not only emphasize the value of the conjunctival test with pure pollen in cases refractory to skin tests,[6] but also suggest the existence of local sensitivity of the mucous membrane in spite of the absence of demonstrable atopic reagins in the blood serum. It may be mentioned here that all of these children exhibited positive skin reactions to other protein substances.

One child who was clinically sensitive to rabbit hair showed, by direct test, a one plus scratch and a two plus intradermal reaction. By indirect test the reactions were negative.

Fourteen children showed positive reactions to house dust. In only two of these was dust an etiologic factor of asthma. One of these two children showed by direct test a four plus scratch reaction and a two plus intradermal reaction. The indirect tests were all negative.

SENSITIZATION TO THE FOOD PROTEINS

Table 2 shows the comparative results of the scratch and intradermal technics with the direct and the indirect methods of skin testing to the common food proteins. It also shows that many of the positive food reactions obtained with the direct method of testing were definitely negative with the indirect method. A few cases will be cited in illustration.

F. W., a girl, aged 7 months, gave a history of marked intolerance to cow's milk. The ingestion of one teaspoonful of a formula made from powdered milk was immediately followed by a violent attack of asthma ending in "status asthmaticus." The infant was admitted to the hospital in this condition. Repeated injections of epinephrine hydrochloride were required to control the asthma. The scratch and intradermal tests with milk by the direct method were both strongly positive. The indirect tests were negative, in spite of the fact that undiluted milk was injected into the serum site. Later, blood was twice drawn from the infant at intervals of three weeks; the serum sites on each occasion showed negative reactions to milk, whereas the direct tests showed persistently strong positive reactions. The serum was injected into several receptive persons other than the mother, and all reacted negatively.

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6. Peshkin, M. M.: Asthma in Children: I. Etiology, Am. J. Dis. Child. **31**:763 (June) 1926.

TABLE 2.—*Corresponding Scratch and Intradermal Reactions to Fifteen Food Substances with the Direct and Indirect (Local Passive Transfer) Methods of Skin Testing*

Skin Reactions	Number of Reactions	Scratch Test: Direct Method						Scratch Test: Indirect Method						Intradermal Test: Direct Method						Intradermal Test: Indirect Method					
														Negative			Positive			Negative			Positive		
		—	±	+	++	+++ and ++++		—	±	+	++	+++ and ++++		—	±	+	++	+++		—	±	+	++	+++	
Wheat																									
±.....	2	2	0	0	0	0		0	0	2	0	0		2	0	0	0	0		2	0	0	0	0	
+.....	2	2	0	0	0	0		1	0	0	1	0		2	0	0	0	0		2	0	0	0	0	
Positive.	4	4	0	0	0	0		1	0	2	1	0		4	0	0	0	0		4	0	0	0	0	
Negative	14	13	0	0	0	1		6	4	2	2	0		14	0	0	0	0		14	0	0	0	0	
Total.	18	17	0	0	0	1		7	4	4	3	0		18	0	0	0	0		18	0	0	0	0	
Corn																									
+.....	1	0	0	1	0	0		0	0	0	1	0		1	0	0	0	0		1	0	0	0	0	
Positive.	1	0	0	1	0	0		0	0	0	1	0		1	0	0	0	0		1	0	0	0	0	
Negative	17	16	0	1	0	0		10	5	2	0	0		16	0	1	0	0		16	0	1	0	0	
Total.	18	16	0	2	0	0		10	5	2	1	0		17	0	1	0	0		17	0	1	0	0	
Rice																									
+.....	1	1	0	0	0	0		1	0	0	0	0		1	0	0	0	0		1	0	0	0	0	
Positive.	1	1	0	0	0	0		1	0	0	0	0		1	0	0	0	0		1	0	0	0	0	
Negative	17	16	1	0	0	0		8	6	3	0	0		16	0	1	0	0		16	0	1	0	0	
Total.	18	17	1	0	0	0		9	6	3	0	0		17	0	1	0	0		17	0	1	0	0	
Rye																									
Positive.	0	0	0	0	0	0		0	0	0	0	0		0	0	0	0	0		0	0	0	0	0	
Negative	18	16	2	0	0	0		15	1	2	0	0		17	0	0	1	0		17	0	0	1	0	
Total.	18	16	2	0	0	0		15	1	2	0	0		17	0	0	1	0		17	0	0	1	0	
Oat																									
±.....	1	1	0	0	0	0		1	0	0	0	0		1	0	0	0	0		1	0	0	0	0	
Positive.	1	1	0	0	0	0		1	0	0	0	0		1	0	0	0	0		1	0	0	0	0	
Negative	17	16	0	0	1	0		14	0	3	0	0		16	0	1	0	0		16	0	1	0	0	
Total.	18	17	0	0	1	0		15	0	3	0	0		17	0	1	0	0		17	0	1	0	0	
Buckwheat																									
Positive.	0	0	0	0	0	0		0	0	0	0	0		0	0	0	0	0		0	0	0	0	0	
Negative	18	17	1	0	0	0		16	1	1	0	0		18	0	0	0	0		18	0	0	0	0	
Total.	18	17	1	0	0	0		16	1	1	0	0		18	0	0	0	0		18	0	0	0	0	
Milk																									
±.....	1	1	0	0	0	0		1	0	0	0	0		1	0	0	0	0		1	0	0	0	0	
++++..	1	1	0	0	0	0		0	0	0	0	1		1	0	0	0	0		1	0	0	0	0	
Positive.	2	2	0	0	0	0		1	0	0	0	1		2	0	0	0	0		2	0	0	0	0	
Negative	16	16	0	0	0	0		11	2	3	0	0		16	0	0	0	0		16	0	0	0	0	
Total.	18	18	0	0	0	0		12	2	3	0	1		18	0	0	0	0		18	0	0	0	0	
Egg																									
±.....	2	1	0	1	0	0		0	0	0	2	0		1	0	0	1	0		1	0	0	1	0	
+.....	2	2	0	0	0	0		0	1	1	0	0		1	0	1	0	0		1	0	1	0	0	
++++..	1	0	0	0	0	1		0	0	0	1	0		0	0	0	0	1		0	0	0	0	1	
Positive.	5	3	0	1	0	1		0	1	1	3	0		2	0	1	1	1		2	0	1	1	1	
Negative	13	12	1	0	0	0		12	1	0	0	0		13	0	0	0	0		13	0	0	0	0	
Total.	18	15	1	1	0	1		12	2	1	3	0		15	0	1	1	1		15	0	1	1	1	
Chicken																									
+.....	1	0	1	0	0	0		0	0	0	1	0		0	0	0	0	1		0	0	0	0	1	
++.....	2	1	1	0	0	0		0	0	0	0	2		1	0	0	0	1		0	0	0	0	1	
Positive.	3	1	2	0	0	0		0	0	0	1	2		1	0	0	0	2		1	0	0	0	2	
Negative	15	14	1	0	0	0		6	7	0	2	0		15	0	0	0	0		15	0	0	0	0	
Total.	18	15	3	0	0	0		6	7	0	3	2		16	0	0	0	2		16	0	0	0	2	
Beef																									
+.....	1	0	1	0	0	0		0	0	0	0	1		1	0	0	0	0		1	0	0	0	0	
++.....	1	1	0	0	0	0		0	0	0	0	1		0	0	1	0	0		0	0	1	0	0	
Positive.	2	1	1	0	0	0		0	0	0	0	2		1	0	1	0	0		0	0	1	0	0	
Negative	16	15	1	0	0	0		13	2	1	0	0		16	0	0	0	0		16	0	0	0	0	
Total.	18	16	2	0	0	0		13	2	1	0	2		17	0	1	0	0		17	0	1	0	0	

TABLE 2.—*Corresponding Scratch and Intradermal Reactions to Fifteen Food Substances with the Direct and Indirect (Local Passive Transfer) Methods of Skin Testing—Continued*

Skin Reactions	Number of Reactions	Scratch Test: Direct Method						Scratch Test: Indirect Method						Intradermal Test: Direct Method						Intradermal Test: Indirect Method					
							+++ and ++++						+++ and ++++	Negative			Positive			Negative			Positive		
		—	±	+	++	+++		—	±	+	++	+++		—	±	+	++	+++	—	±	+	++	+++		
Lamb																									
+.....	2	2	0	0	0	0	0	0	0	0	0	2	2	2	0	0	0	0	2	0	0	0	0	0	0
Positive.	2	2	0	0	0	0	0	0	0	0	0	2	2	2	0	0	0	0	2	0	0	0	0	0	0
Negative	16	16	0	0	0	0	0	12	3	1	0	0	0	15	0	1	0	0	15	0	1	0	0	0	0
Total.	18	18	0	0	0	0	0	12	3	1	0	2	2	17	0	1	0	0	17	0	1	0	0	0	0
Pork																									
±.....	1	1	0	0	0	0	0	0	1	0	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0
Positive.	1	1	0	0	0	0	0	0	1	0	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0
Negative	17	16	1	0	0	0	0	12	4	0	1	0	0	16	1	0	0	0	16	1	0	0	0	0	0
Total.	18	17	1	0	0	0	0	12	5	0	1	0	0	17	1	0	0	0	17	1	0	0	0	0	0
Peanut																									
Positive.	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Negative	17	17	0	0	0	0	0	16	0	1	0	0	0	17	0	0	0	0	17	0	0	0	0	0	0
Total.	17	17	0	0	0	0	0	16	0	1	0	0	0	17	0	0	0	0	17	0	0	0	0	0	0
Almond																									
+.....	1	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0	1	0	0
Positive.	1	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0	1	0	0
Negative	17	17	0	0	0	0	0	15	1	1	0	0	0	17	0	0	0	0	17	0	0	0	0	0	0
Total.	18	17	0	0	1	0	0	15	1	1	1	0	0	17	0	0	1	0	17	0	0	0	1	0	0
Mustard																									
±.....	1	1	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0
+.....	1	1	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0
++.....	2	0	0	0	0	2	0	0	1	1	0	0	0	2	0	0	0	0	2	0	0	0	0	0	0
++++..	1	0	0	0	0	1	1	1	0	0	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0
Positive.	5	2	0	0	0	3	2	2	1	2	0	0	0	5	0	0	0	0	5	0	0	0	0	0	0
Negative	13	13	0	0	0	0	0	10	2	1	0	0	0	12	0	1	0	0	12	0	1	0	0	0	0
Total.	18	15	0	0	0	3	2	12	3	3	0	0	0	17	0	1	0	0	17	0	1	0	0	0	0

A. L., a boy, aged 1½ years, showed positive scratch and intradermal reactions when the direct method was used in testing with beef, chicken and lamb; when the indirect method of testing was used, the scratch tests were all negative, and the intradermal tests were negative to lamb and positive to beef and chicken. Immediately following the intradermal tests (direct method) a general reaction ensued, manifested by a generalized erythema and urticaria.

J. F., a boy, aged 12 years, showed by direct test positive scratch and intradermal reactions with beef, chicken and lamb; following the intradermal tests, a violent attack of asthma with generalized urticaria occurred. By the indirect method, the intradermal tests were all negative, and the scratch tests were negative to lamb and positive to chicken and beef.

Table 3 is a summary of the corresponding scratch reactions with the direct and indirect methods of skin testing to all the food and inhalant substances used in this series.

The total number of positive reactions (± to +++) obtained by the scratch technic with the direct method of skin testing was ninety-two. Of this number only eighteen reactions, or 19.5 per cent, were found positive with the indirect method.

The total number of negative tests by the direct method of skin testing was 496. Of this number, 12 tests, or 2.4 per cent, showed reactions positive with the indirect method.

Table 4 is a summary of the corresponding intradermal reactions with the direct and indirect methods of skin testing to all the food and inhalant substances used in this series.

The total number of definitely positive reactions (+ + and + + +) obtained by the intradermal technic with the direct method

TABLE 3.—*Summary of the Corresponding Scratch Reactions with the Direct and Indirect (Local Passive Transfer) Methods of Skin Testing to Thirty-Three Food and Inhalant Substances*

Direct Method		Indirect Method				
Skin Reactions	Number of Reactions	—	±	+	++	+++ and ++++
+	36	31	2	2	1	0
++	12	8	1	0	1	2
+++ and ++++....	7	3	0	0	0	4
Plus reactions	55	42	3	2	2	6
Plus-minus reactions.	37	32	3	1	0	1
Positive	92	74	6	3	2	7
Negative	496	484	9	1	1	1
Total	588	558	15	4	3	8

TABLE 4.—*Summary of the Corresponding Intradermal Reactions with the Direct and Indirect (Local Passive Transfer) Methods of Skin Testing to Thirty-Three Food and Inhalant Substances*

Direct Method		Indirect Method				
		Negative			Positive	
Skin Reactions	Number of Reactions	—	±	+	++	+++
++	24	14	1	3	4	2
+++	10	7	0	1	1	1
Positive reactions.....	34	21	1	4	5	3
One plus reactions....	70	58	0	10	2	0
Plus-minus reactions .	86	83	2	1	0	0
Negative	398	393	2	3	0	0
Total reactions....	588	555	5	18	7	3

of testing was thirty-four. The corresponding indirect tests showed positive reactions in eight instances, or 23.5 per cent, one plus in four instances, or 12 per cent, and negative (— and ±) in twenty-two instances, or 64.5 per cent.

The total number of one plus reactions with the direct method was seventy. The corresponding tests with the indirect method were negative in fifty-eight instances, or 83 per cent.

The total number of plus reactions (+ to + + +) with the direct method was 104. The corresponding tests with the indirect method showed plus reactions in only twenty-four instances, or 23 per cent.

The total number of negative reactions with the direct method was 484. The corresponding tests with the indirect method showed plus reactions in four instances, or 0.82 per cent.

It would appear that the plus-minus and one plus reactions obtained by the intradermal technic with the indirect method of testing do not have any more special significance than the same reactions obtained by the direct method.

Table 5 is a summary of the corresponding scratch and intradermal reactions, with the direct and indirect methods of skin testing, to all the protein substances employed in this series.

The total number of plus reactions (+ to + + + +) obtained by the scratch technic with the direct method of skin testing was fifty-five; the corresponding tests with the intradermal technic showed defi-

TABLE 5.—*Summary of the Corresponding Scratch and Intradermal Reactions to Thirty-Three Food and Inhalant Substances with the Direct and Indirect (Local Passive Transfer) Methods of Skin Testing in Eighteen Children with Asthma*

	Direct Method						Indirect Method								
	Scratch Test			Intradermal Test			Scratch Test					Intradermal Test			
		Negative			Positive							Negative			Positive
Skin Reactions	No. of Reactions	—	±	1+	2+	3+	—	±	1+	2+	3+ and 4+	—	±	1+	2+	3+
+	36	11	6	5	9	5	31	2	2	1	0	29	1	3	2	1
++	12	0	2	7	2	1	8	1	0	1	2	10	0	1	0	1
+++ and ++++	7	1	0	0	4	2	3	0	0	0	4	4	0	0	2	1
One to four plus	55	12	8	12	15	8	42	3	2	2	6	43	1	4	4	3
Plus minus	37	15	7	11	4	0	32	3	1	0	1	33	0	2	2	0
Total positive	92	27	15	23	19	8	74	6	3	2	7	76	1	6	6	3
Negative	496	371	71	47	5	2	484	9	1	1	1	479	4	12	1	0
Total tests	588	398	86	70	24	10	558	15	4	3	8	555	5	18	7	3

nitely positive (+ + and + + +) reactions in twenty-three instances, one plus in twelve and negative (± and —) reactions in twenty instances, or 36 per cent. By the indirect method with the scratch technic, the tests showed positive (± to + + + +) reactions in thirteen instances and negative reactions in forty-two instances, or 76 per cent; with the intradermal technic, the tests showed definitely positive reactions in seven instances, one plus in four and negative in forty-four instances, or 80 per cent.

The total number of positive reactions (± to + + + +) obtained by the scratch technic with the direct method was ninety-two; the corresponding tests with the intradermal technic showed definitely positive reactions in twenty-seven instances, one plus in twenty-three and negative in forty-two instances, or 45.6 per cent. By the indirect method with the scratch technic, the tests showed positive reactions in only eighteen and negative in seventy-four instances, or 80 per cent; with the intradermal technic, the tests showed definitely positive reac-

tions in only nine instances, one plus in six and negative in seventy-seven instances, or 83.7 per cent.

The total number of negative reactions obtained by the scratch technic with the direct method was 496; the corresponding tests with the intradermal technic showed definitely positive reactions in 7 instances, one plus reactions in 47 and negative reactions in 442 instances, or 89 per cent. By the indirect method with the scratch technic, the tests showed positive reactions in 12 and negative in 484 instances, or 97 per cent; with the intradermal technic, the tests showed definitely positive reactions in only 1 instance, one plus in 12 and negative in 483 instances, or 97 per cent.

With the indirect method of skin testing, the total number of control tests performed with both the scratch and the intradermal technics was 1,176. With the scratch technic, positive reactions occurred in 3 instances, or 0.5 per cent. With the intradermal technic definitely positive reactions occurred in 4 instances, or 0.7 per cent and one plus reactions in 12 instances, or 2 per cent.

It may be mentioned that the control tests with the powdered extract of house dust yielded positive reactions with the scratch technic in two of the eighteen persons passively sensitized, a plus-minus reaction in the one case and a one plus in the other. With a concentrated fluid extract of house dust employed intradermally, the control tests yielded a two plus reaction in three subjects, a one plus reaction in five and a plus-minus reaction in two. In all of these persons, a history of intolerance to house dust was lacking.

Gay and Chant [7] found that sensitization could be demonstrated "for as long as thirty-six days after the injection of the sensitizing serum" (intradermal technic). In this study it was found that with the scratch technic, passively sensitized serum sites yielded maximum positive reactions for a period of from two to three weeks. After this time the skin reactions obtained became progressively smaller, and at the end of from four to five weeks the reactions disappeared. With the intradermal technic, serum sites yielded maximum positive reactions for a period of one month, after which the reactions became progressively smaller and at the end of from five to seven weeks were negative. Sterile sensitizing blood serum kept under proper conditions was found to retain its power to sensitize for at least one month.

COMMENT

The factors that influence the presence or absence of "atopic reagins" (specific sensitizing substances) in the blood of persons with asthma or hay-fever are not known. Whether reagins develop prior to, along

7. Gay, L., and Chant, E.: Passive Transfer of Hypersensitivity, Bull. Johns Hopkins Hosp. **40**:270 (May) 1927.

with, or after, the establishment of sensitiveness of the skin or mucous membrane is still to be determined. The existence of hypersensitiveness of the nasal or bronchial mucous membrane without sensitivity of the skin is established. In our study, this type of case also failed to show the presence of reagins. Patients have been observed who showed positive reactions to pollen by the skin and conjunctival tests as well as by the presence of specific reagins in the blood without any clinical symptoms of hay-fever.

A patient with asthma resisting all forms of therapy may become free from symptoms for a considerable period after an acute infection. The onset of asthma may also follow any one of the acute diseases incident to childhood.[8] It is therefore probable that an acute infection, such as pneumonia, or an exanthem may either alter or stimulate the formation of atopic reagins in the blood sufficiently to induce, aggravate or relieve asthma. One child with allergy became free from symptoms after developing measles. This child was tested five days after the temperature had returned to normal. The skin reactions obtained with both the direct and the indirect methods were the same as those obtained before measles was contracted. In this case, although the symptoms of asthma were relieved, the specific reagins seemed to be unchanged.

The phenomenon of local passive transfer of hypersensitiveness is an important contribution to the advancement of the science of allergy. The present knowledge, however, concerning the origin and nature of "atopic reagins" in the blood of patients with symptoms of asthma or hay-fever is far from complete. While the presence of specific reagins in many of these patients can be demonstrated, the employment of this procedure in a routine manner for the determination of etiologic factors of asthma is unreliable, and its application as a substitute for the direct method of skin testing even in specially selected cases is, in our experience, impracticable.

CONCLUSIONS

1. The application of local passive transfer of human hypersensitiveness as a means of testing (indirect method) has been compared with the accepted technics (scratch and intradermal) of skin testing (direct method).

2. Eighteen children with asthma ranging in age from 7 months to 14 years were each tested by the direct and indirect methods with thirty-three protein extracts, both the scratch and intradermal technics being used. Dry powdered extracts were employed for the scratch and routine fluid extracts (Coca) for the intradermal tests. All of these children were under observation for two years.

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8. Peshkin, M. M.: Asthma in Children: III. The Incidence and Significance of Various Diseases and Infections, and of Tonsillectomy and Adenoidectomy, Am. J. Dis. Child. **33**:880 (June) 1927.

3. The total number of tests performed exclusive of confirmatory and control tests was 2,352.

4. The total number of positive reactions (± to ++++) obtained by the scratch technic with the direct method was ninety-two. Of this number only eighteen reactions, or 19.5 per cent, were found positive with the indirect method.

5. The total number of plus reactions (+ to +++) obtained by the intradermal technic with the direct method was 104. The corresponding tests with the indirect method showed plus reactions in only 24 instances, or 23 per cent.

6. Comparative tests between the scratch and intradermal technics with both the direct and the indirect methods show that the total number of positive reactions obtained by the scratch technic with the direct method was ninety-two; of these, 80.5 per cent were negative with the indirect method. The corresponding tests with the intradermal technic by the direct method showed fifty plus reactions; of these, 83.5 per cent were negative with the indirect method.

The total number of negative reactions obtained by the scratch technic with the direct method was 496; of these, 3 per cent were positive with the indirect method. The corresponding tests with the intradermal technic by the direct method showed negative reactions in 442 instances and plus reactions in 54; of these, 3 per cent were positive with the indirect method.

7. Cases showing definitely positive skin reactions with substances such as milk, chicken, beef, lamb, rabbit hair, timothy and ragweed pollen by the direct method, in which these substances were clinically proved etiologic factors of asthma, failed to give positive reactions with the indirect method.

8. Three children with asthma and hay-fever reacted negatively to pollen with both the direct and the indirect methods of skin testing (the fluid extract for the intradermal test was employed up to a concentration of 0.25 mg. of nitrogen per cubic centimeter); they gave, however, positive reactions by the conjunctival test with the dry powder. This again emphasizes the value of the latter technic of testing which has been shown by one of us [6] to be a rapid, safe and reliable method of demonstrating sensitiveness to pollen in patients refractory to skin tests.

9. The indirect method of testing (scratch and intradermal technics) employed as a routine measure to determine etiologic sensitizations in children with allergy is unsatisfactory. Its employment as a substitute for the direct method of testing even in specially selected cases is, in our experience, impractical.

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A COMPARISON OF THE CALCULATED AND DETERMINED OSMOLAR CONCENTRATION OF NORMAL SERUM

THE BASE-BINDING POWER OF PROTEINS AND THE DETERMINATION OF TOTAL BASE *

DAN C. DARROW, M.D.
AND
ALEXIS F. HARTMANN, M.D.
WITH THE TECHNICAL ASSISTANCE OF MARIE MORTON
ST. LOUIS

Recent observations made in different laboratories have emphasized the fact that the total electrolyte content of the blood plasma, and presumably of the body fluids in general, tends to be maintained at a relatively constant level in spite of wide variations in the concentrations of individual ions, and in spite of large fluctuations of plasma water content.

In experimental pyloric obstruction, Gamble and Ross [1] called particular attention to the fact that the total base of the plasma is altered but slightly when enormous reduction of chloride and increase of bicarbonate occur. A similar deduction was made by Hartmann and Smyth [2] in their study of pyloric stenosis, intestinal obstruction, intestinal fistula and persistent vomiting due to parenteral infections in infants and children. In these conditions, it was apparent that the maintenance of total electrolyte (or fixed base, as expressed by Gamble) took precedence over the maintenance of the normal hydrogen-ion concentration, and persistent uncompensated alkalosis often resulted. Gamble, Ross and Tisdall [3] also showed that, during fasting, the loss of weight and, presumably, the reduction of tissue cell volume due to consumption of glycogen is accompanied by an excretion of fixed base, acid and water in such proportions that the fixed base of the body is maintained at the normal concentration in the remaining body water. Darrow and Buckman [4] showed that the electrolyte content and osmotic pressure of the

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* From the Department of Pediatrics, Washington University School of Medicine, and the St. Louis Children's Hospital.

1. Gamble, J. L., and Ross, G. S.: J. Clin. Investigation **1**:403, 1925.

2. Hartmann, A. F., and Smyth, F. S.: Chemical Changes in Body Occurring as Result of Vomiting, Am. J. Dis. Child. **32**:1 (July) 1926.

3. Gamble, J. L.; Ross, G. S., and Tisdall, F. F.: J. Biol. Chem. **57**:633, 1923.

4. Darrow, D. C., and Buckman, T. E.: The Volume of the Blood: II. The Volume of the Blood and Concentration and Crystalloids and Electrolytes in Dehydration and Edema, Am. J. Dis. Child. **36**:248 (Aug.) 1928.

serum are relatively constant despite fairly great reduction of the plasma volume in cases of anhydremia due to diarrhea and in cases of nephrosis with edema.

Peters, Bulger, Eisenman and Lee,[5] in their studies of diabetes and nephritis of adults, showed that significant reduction of body chloride and bicarbonate may occur in the presence of an increase in the other acid ions, and that under these circumstances, the total base remains almost normal. They felt that the chloride ion shifted in response to an increase of the organic acid ions just as much as the bicarbonate ion did, and objected to Gamble's conferring of the "mendicant position" solely to bicarbonate. Essentially similar observations were made by Hartmann and Darrow[6] in children with nephritis. It was pointed out, however, that a marked decrease in the total electrolyte (or fixed base) concentration frequently occurred without being accompanied by a corresponding reduction of the osmotic pressure of the serum. In such cases, the decrease in electrolyte was compensated for osmotically by an increase of nonelectrolyte (chiefly urea). A similar maintenance of the osmotic pressure of the serum by retention of nonelectrolyte when electrolyte loss occurred was noted by Hartmann and Smyth[2] in cases without nephritis in which the loss of electrolyte and fixed base occurred by way of the gastro-intestinal secretions. It seems likely, therefore, that the maintenance of the osmotic pressure of the body fluids takes precedence over the maintenance of the electrolyte concentration just as the latter takes precedence over the maintenance of the hydrogen-ion concentration.

The observations reported in the present paper were made on the serums of normal persons to establish the relationship of the total electrolyte and nonelectrolyte concentrations to the osmotic pressure as determined by the depression of the freezing point. In order to compare electrolyte with nonelectrolyte and with the depression of the freezing point, the results of all determinations are expressed in terms of osmolar concentration.

METHODS

The blood was collected under oil and allowed to clot and all determinations were made on the serum, except for a few dextrose, lactic acid and nonprotein nitrogen estimations made on oxalated whole blood. The results are given in the accompanying table. Acids and total base are expressed as milli-equivalents of univalent base per volume. The osmolar concentration is expressed in millimols of undissociated crystalloid, a correction for the volume of water being used as suggested by

5. Peters, J. P.; Bulger, H. A.; Eisenman, A. J., and Lee, C.: J. Clin. Investigation **2**:167, 1925.

6. Hartmann, A. F., and Darrow, D. C.: J. Clin. Investigation **6**:127, 1928.

*Concentration of Principal Crystalloids of Serum**

			Acid-Base Concentration by Volume							Osmolar Concentration					
Case	Age	p_H	BCl, M-eq.	$BHCO_3$, M-eq.	B—Protein, M-eq.	BH_2PO_4 + B_2HPO_4, M-eq.	B—Lactate, M-eq.	Total Acid, M-eq.	Total Base, M-eq.	Dextrose, Millimols	Urea, Millimols	Total Electrolyte, Millimols	Total Calculated = C, Millimols	Freezing Point = F, Millimols	C / F per Cent
1	1 mo.	7.42	97	22.2	15.8	3.2	2.7	140.9	151	4.7	9.1	277	291	309	94.6
2	7 mo.	7.39	105	21.4	12.6	2.8	0.7	143.5	147	5.0	6.6	273	285	309	92.5
3	11 mo.	7.37	101	21.4	13.9	1.7	3.6	141.6	...	4.7	6.4	280	291	304	96.0
4	13 mo.	(7.40)	101	25.4	10.9	2.6	2.4	142.3	154	6.0†	7.9	273	287	...	....
5	3.5 yr.	7.47	102	24.4	13.7	2.9	2.8†	145.8	...	(6.0)	6.2	274	286	325	88.4
6	4 yr.	7.47	101	24.8	16.8	1.2	2.7	146.5	150	6.0	5.6	281	292	324	90.5
7	8 yr.	7.42	98	25.8	14.9	2.8	2.2	143.5	151	5.3	9.7	272	287	327	88.4
8	9 yr.	7.35	96	20.7	21.0	(2.0)	2.3	152.0	151	11.0	3.8	274	288	...	....
9	9 yr.	7.46	103	23.9	15.4	2.4	2.3	147.2	151	4.7	6.6	278	289	...	....
10	11 yr.	7.45	98	28.7	15.2	2.3	1.5	145.7	159	8.5	7.1	280	294	316	93.5
11	28 yr.	7.45	99	26.0	16.7	1.7	2.2	145.6	145	7.3	8.0	277	293	322	91.3
12	31 yr.	7.46	102	28.2	16.3	1.7	2.5	150.7	151	7.3	7.3	291	306	325	94.4
13	32 yr.	7.45	99	28.2	15.3	1.7	1.3	145.5	148	5.9	6.7	277	290	326	89.3
Maximum			105	28.7	21.0	3.2	3.6	152.0	159	11.0	9.7	291	306	326	96.0
Minimum			97	20.7	10.9	1.2	0.7	141.0	145	4.7	3.8	271	285	304	88.4
Average			100	24.7	15.2	2.2	2.2	145.0	150.7	6.3	6.9	277	290	319	92.1

* In this table M-eq. indicates milli-equivalent.

† Determination made on oxalated whole blood.

( ) assumed value.

Van Slyke, Wu and McLean.[7] The depression of the freezing point was divided by 0.00184 to express milli-osmolar concentration.[8]

In converting the total carbon dioxide content into equivalent $BHCO_3$, it was assumed that $\frac{1}{21}$ of the carbon dioxide represented free carbonic acid. This method of calculation does not take into account the variations in the p_H, but such an omission introduces no significant error. The base-binding power of protein was determined by the equation of Hastings, Salvesen, Sendroy and Van Slyke[9] which is $(BP) = 0.097\ (p_H - 5.26)$. (BP) is the base-binding power of serum protein and p_H, the p_H of the serum. The inorganic phosphate concentration was converted into its equivalent base-binding power at p_H 7.4 ($1.8 \times$ the millimolar concentration of $HPO_4^=$).

In converting the concentration of acids into osmolar concentration, it was thought best to use the osmolar concentrations indicated by determinations of the freezing point. The extent of the ionization of salts at 38 C. is not that indicated by the freezing point, but the calculation based on the molecular depression of the freezing point of salts permits the direct comparison with the concentration indicated by the freezing point of the serum. The tables of Lanboldt and Börnstein[10] were used, choosing the concentration nearest that of the given salt in the serum. In all cases, the sodium salt of the acid was chosen. The molecular depression of the freezing point was considered 1.84 C. in converting

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7. Van Slyke, D. D.; Wu, Hsien, and McLean, F. C.: J. Biol. Chem. **56**:765, 1923.

8. The methods used are as follows:

   p_H: Hastings, A. B., and Sendroy, J.: J. Biol. Chem. **61**:95, 1924.
   Chlorides: Van Slyke, D. D.: J. Biol. Chem. **58**:523, 1923.
   Carbon dioxide: Van Slyke, D. D., and Cullen, J. E.: J. Biol. Chem. **30**:289, 1917.
   Protein, refractometrically: Reiss, E.: Ergeb. d. inn. Med. u. Kinderh. **10**:532, 1913.
   Phosphate: Briggs, A. P.: J. Biol. Chem. **59**:255, 1924.
   Lactic acid: Friedman, T. E.; Cotonio, M., and Shaffer, P. A.: J. Biol. Chem. **73**:335, 1927.
   Total base: Stadie, W. C., and Ross, E. C.: J. Biol. Chem. **65**:735, 1925.
   Sugar: Shaffer, P. A., and Hartmann, A. F.: J. Biol. Chem. **45**:349, 1921.
   Nonprotein nitrogen: Folin, O., and Youngberg, G. E.: J. Biol. Chem. **38**:111, 1919.
   Freezing point: Darrow, D. C., and Buckman, T. E.: The Volume of Blood: I. The Use of Thermocouple for Determining the Freezing Point of a Small Quantity of Fluid, Am. J. Dis. Child. **36**:78 (July) 1928.

9. Hastings, A. B.: Salvesen, H. A.; Sendroy, J., and Van Slyke, D. D.: J. Gen. Physiol. **8**:701, 1927.

10. Landoldt, Börnstein: Physikalisch-Chemischer Tabellen, Springer, Berlin, 1912.

the molecular depression of the freezing point of salts into osmolar concentration. On this basis the milli-osmolar concentrations of the acids are obtained by multiplying the respective milli-equivalent concentration by the following factors: (1) $[BCl] \times 1.87$, (2) $[BHCO_3] \times 1.95$, (3) $[BH_2PO_4 + B_2HPO_4] \times 1.77$ and, (4) $[BC_3H_5O_3]$ (lactate) was assumed to dissociate to the same extent as sodium chloride, giving a factor of 1.87. A reliable figure could not be found for the depression of the freezing point brought about by proteins. Proteins probably affect the freezing point of salt solutions in two ways: (1) by their own molecular concentrations and that of the salts they form, and (2) by changing the water and salt concentration of the solution by adsorption. In the absence of any evaluation of these factors, the molecular concentration was assumed to be that of the base-binding power of the protein. This may be either too high or too low, but probably is approximately correct.

All the values for the osmotic concentration were corrected for the volume of water. This was assumed to be given by the formula of Van Slyke, Wu and McLean [7] which is $W = 0.99 - 0.8\ P$. W is the water content of the serum and P, the protein content of the serum in grams per hundred cubic centimeters. This value has been checked by drying serum at 110 C., and found to be surprisingly accurate in measuring the dried residue. Nevertheless, this formula almost certainly indicates a water concentration greater than actually exists at 37 C., for less and less water is bound to the protein, the higher the temperature. However, this correction will not be misleading if one keeps in mind that later work will probably show it to be too small. The copper reducing substances were assumed to be dextrose, and 0.7 of the nonprotein nitrogen to be urea nitrogen. The latter is probably too high a figure for normal blood, but no value was assigned for the nonprotein nitrogen which is not urea. The total calculated osmolar concentration does not take into account the excess of the base over determined acids.

The serums were obtained from essentially normal persons. It will be noticed from the table that there is a fairly constant excess of base over determined acids of about 5 milli-equivalents. This agrees well with the figure for organic acids found by Perlzweig and Delrue.[11] Including lactic acid, they found from 5 to 8 milli-equivalents in normal persons by electrometric titration. Furthermore, in all probability 1 or 2 milli-equivalents of calcium are bound with the protein in excess of that indicated by the formula of Hastings, Salvesen, Sendroy and Van Slyke.[9] In deriving their formula, protein was dialyzed and assumed to be base free, but presumably a small amount of calcium remained bound

11. Perlzweig, W. A., and Delrue, G.: Proc. Soc. Exper. Biol. & Med. **25**:548, 1928.

to the protein on dialysis. The formula gives the amount of sodium bound to protein in a NaCl + NaH CO_3 solution at varying tensions of carbon dioxide and does not take into account the calcium which can not be entirely separated from the protein by dialysis.

It will be noticed that the osmolar concentration of the electrolyte averages 277 millimols. The greatest variation observed was only 7 per cent from the average while the usual was less than 2 per cent. Since electrolyte accounts for 87 per cent of the osmolar concentration of the serum estimated from the freezing point, the constancy of the electrolyte concentration accounts for the constancy of the freezing point. The average of the total osmolar concentration calculated from the determined acids, dextrose and nonprotein nitrogen is 290 millimols. In one instance, a 5.5 per cent variation from the average was noted, but in the remaining instances the difference was less than 2 per cent. This average "mol-rest" is equivalent to 20 millimols of undissociated substance, or 11 milli-equivalents of a highly dissociated salt.

The average observed excess of total base over total acid will account for about one half of the "mol-rest," if we assume that the undetermined electrolyte exists as a highly dissociated salt. Except for 1 milli-equivalent each of sulphuric and amino acid, little is known as to the nature of the acids forming salts with this excess of base. Furthermore, as already pointed out, the correction for the volume occupied by the solute (particularly protein) is probably too small. If so, the calculated osmolar concentration would be in almost perfect agreement with the observed.

The average depression of the freezing point of true venous serum is —0.587 C., while the usually accepted average [12] has been —0.565 C. This may be explained by the fact that the determinations were made on serum of venous blood collected and separated under oil, while usually no attempt has been made to prevent loss of carbon dioxide and the accompanying shift of chloride and water from the cell to the serum. Eisenman, Bulger and Peters [13] found on changing the carbon dioxide tension of defibrinated blood from 30 to 60 mm. of mercury, an average increase of 5 in the milli-osmolar concentration of the serum electrolyte, with an accompanying change in the $BHCO_3$ concentration of 5 milli-equivalents. This agrees well with some unpublished experiments by Darrow and Buckman in which a change in the carbon dioxide content was accompanied by a change in the freezing point of about 0.001 degree for each per cent by volume change in the carbon dioxide. Therefore, neglecting to prevent the loss of carbon dioxide while the serum is in

12. Gram, H. C.: J. Biol. Chem. **56**:593, 1923 (footnote 4).

13. Eisenman, F. J.; Bulger, H. A., and Peters, J. P.: J. Biol. Chem. **67**:159, 1926.

contact with the red cells may easily account for a raising of the freezing point of 0.02 to 0.03 C.

It was found that the freezing point of serum separated from the cells did not change appreciably on standing two days in the icebox.

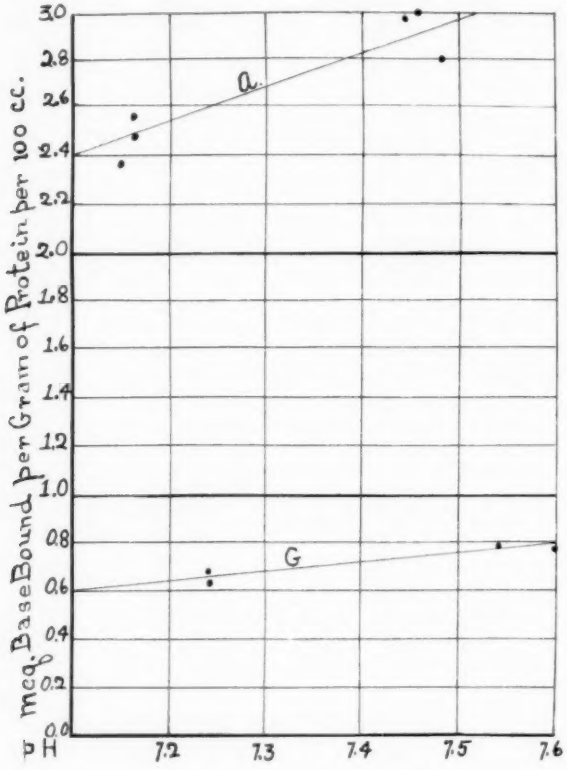
It seems probable that in pathologic bloods the base-binding power of serum protein is not the same as that given by the formula of Hastings, Salvesen, Sendroy and Van Slyke. For this formula to apply accurately, the serum must have the same proportion of albumin and globulin as that used in deriving the formula. Globulins bind less base than albumins, and formulas taking into consideration the albumin and globulin concentrations would be desirable. In order to derive such formulas, the following work was undertaken.

Beef blood was collected and the serum separated within two hours. The serum dialyzed in closed collodion sacs against distilled water in an atmosphere of carbon dioxide for from two to three days in the cold. This caused a precipitation of the water-insoluble globulins. In each experiment, chloride or nonprotein nitrogen could not be detected in the dialyzed serum. There remained, however, a faint trace of phosphate and from 1 to 2 milli-equivalents of calcium. The base-binding power of the dialyzed serum was determined as described by Van Slyke, Wu and McLean[7] on: (1) the whole serum, (2) the washed precipitated globulins and (3) the proteins not precipitated by dialysis. Protein was determined by the gross Kjeldahl method using the factor 6.25 and albumin and globulin similarly after precipitation by 22.2 per cent disodic sulphate. The p_H was calculated from the carbon dioxide content and carbon dioxide tension using the factors suggested by these authors. The data obtained are represented in the chart.

The base-binding power of the globulins was found to be (BG) $= 0.4\ p_H - 2.24)$ G. (BG) is the base bound to globulin in milli-equivalents per volume, G is the grams of globulin per 100 cubic centimeters and p_H is the p_H of the serum. The base-binding power of the albumin was found by assuming that the globulin not precipitated during dialysis had the same base-binding power as the globulin precipitated during dialysis. Thus, knowing the concentrations of albumin and globulin together with the base-binding power of a sample of serum, one may calculate the base-binding power of the albumin. The formula for this is (BA) $=$ (1.411 $p_H - 7.65$ A. (BA) is base bound by albumin in milli-equivalents per volume, A is the grams of albumin per 100 cubic centimeters, and the p_H is the p_H of the serum. Thus, in a given serum, one adds the value of the base bound to albumin and the base bound to globulin to obtain the base bound to protein.

In certain cases of nephrosis the total acids and total base are the same when using the formula of Hastings, Salvesen, Sendroy and Van Slyke. The change in the ratio of albumins to globulins, however,

lowers the value for the base bound to proteins so that one finds the usual 5 milli-equivalents of excess base over acid on using the above formulas. The following is an example of a typical case of lipoid nephrosis. The total base was 146 millimols. Using the formula of Hastings and others for the base bound to protein, the total acid was 148 millimols, but using the separate formulas for globulin or albumin, the total acid is only 143 millimols.



A indicates the curve for albumin; (BA) = (1.41 p_H — 7.65)A, and G, the curve for globulin (BG) = (0.4p_H — 2.24)G.

The formulas are probably not exact, for the base-binding power of albumin is derived by subtracting a value for the globulins not precipitated by dialysis which may not be correct for all the globulins. In cases with abnormal proportions of albumin and globulin, however, it is more accurate than the formula of Hastings and others. An attempt to obtain a value for albumin by complete precipitation of the globulins with ammonium sulphate and subsequent dialysis gave values that were obviously incorrect. Apparently such treatment altered the character of the proteins.

A NOTE ON THE DETERMINATION OF TOTAL BASE

Peters, Bulger, Eisenman and Lee [14] reported figures essentially the same as those in this paper. Their average values for undetermined acid is 12 milli-equivalents, but their greater value is accounted for in part by the 2 milli-equivalents lower figure for the base-binding power of proteins given by the formula which they used and the fact that the 2 milli-equivalents of lactic acid are included in their excess of base over acid. They did not remove phosphate, but added 1 milli-equivalent of base for each millimol of phosphate.

Suderman, Austin and Camac [15] gave values essentially the same as those in this paper. They did not determine lactic acid or inorganic phosphate, but after assigning the same value for the base-binding power of proteins as that used in this paper, and 4 milli-equivalents for phosphate and lactic acid, their data show an average excess of base over acid of 3 milli-equivalents. Hamilton [16] and Blackfan and Hamilton [17] reported values about 8 milli-equivalents higher than those of this paper. They removed phosphate. Schiff, Bayer and Tukuyama [18] reported extremely high figures, from 160 to 200 milli-equivalents on normal children. They removed phosphate and titrated an aliquot equivalent to only 0.2 cubic centimeters of serum. Their values do not seem to be correct, since that much base, if actually present, would produce a greater depression of the freezing point than that of normal serum. The total base concentrations of Hamilton are possible, but it does not seem likely that there are 12 milli-equivalents of undetermined acids when the average undetermined osmolar concentration is only 20 millimols. This can only be possible if too high osmolar concentrations have been assigned to the various salts. As pointed out, this may be the case with proteins, but is unlikely for the other salts, sugar or nonprotein nitrogen.

Experimental determinations of total base in known solutions of sodium chloride of approximately 150 millimols concentration to which sodium biphosphate U. S. P. was added in concentrations varying from 2.5 to 20 milli-equivalents of univalent base, have convinced us that the method of Stadie and Ross is accurate without correction for phosphate. The serum was ashed and ignited in pyrex beakers without the removal

14. Peters, J. P.; Bulger, H. A.; Eisenman, A. J., and Lee, C. J.: J. Biol. Chem. **67**:141, 1926.

15. Suderman, W. F.; Austin, J. H., and Camac, J. G.: J. Clin. Investigation **3**:37, 1926.

16. Hamilton, B.: J. Biol. Chem. **65**:101, 1925.

17. Blackfan, K. D., and Hamilton, B.: Bull. Johns Hopkins Hosp. **45**:322, 1927.

18. Schiff, E.; Bayer, W., and Tukuyama, M.: Jahrb. f. Kinderh. **69**:161, 1928. Schiff, E.; Bayer, W., and Karelitz: ibid. **68**:17, 1927.

of phosphate. The beakers were not heated to red heat for longer than from one-half to one minute in one place. This left only about 0.5 cubic centimeters of fiftieth normal sulphuric acid, and avoided the danger of fusing the ash or dissolving base from the glass in appreciable quantities.

Addition of 5 milli-equivalents of calcium chloride also gave theoretical results. Apparently the benzidine reagent precipitates the phosphate. These analyses were repeated several times during the past three years, with the same results, which would indicate that there should be no phosphate correction. Furthermore, attempts to remove phosphate as described by Stadie and Ross usually gave results that were high by from 5 to 10 milli-equivalents, though sometimes they were correct. The impression is that one cannot be sure that the phosphate removal will not give high results and the correction of 1 equivalent for each millimol of phosphate is not necessary. The difference in the results obtained in this laboratory and elsewhere probably has to do with the length of heating and conversion of phosphate into metaphosphate. Some of the results reported here may be slightly low, but they are probably more nearly correct than those after phosphate removal.

SUMMARY

Determinations of p_H, chloride, bicarbonate, protein, inorganic phosphate, lactic acid, total base, sugar, nonprotein nitrogen and freezing point were made on the serums of thirteen normal persons.

A method of calculating the milli-osmolar concentration of the determined acids plus sugar and urea was developed.

The concentration indicated by these calculations accounts for about 92 per cent of the milli-osmolar concentraion indicated by the depression of the freezing point. Reasons are given for believing that little osmotically active substance can exist in the normal serum that is not accounted for in the foregoing determinations.

Separate formulas are given for the base-binding power of serum albumin and serum globulin. It is suggested that these formulas are more accurate in cases with a disturbance of the albumin-globulin ratio than the formulas previously used.

OSSIFICATION AND GROWTH OF CHILDREN FROM ONE TO EIGHT YEARS OF AGE*

RUTH OTIS SAWTELL, PH.D.
Anthropologist, Bureau of Educational Experiments
NEW YORK

The purpose of this article is to show the progress and variation of ossification and growth in the hands of young children, the interrelation of these processes and their significance in respect to other physiologic traits.

As part of the data for the five year study of mental and physical growth of the preschool child, the Bureau of Educational Experiments in New York undertook the collection of roentgenograms of the hand and forearm of each child in Groups 3 to 6 of the City and Country School and the Bureau's own Nursery School. The material here employed represents that collected during a three-year period, from January, 1925, through November, 1927. The roentgenograms were taken at intervals of three months throughout the school year, a program still in operation, with the addition, for a later study of skeletal relationships, of pictures of the foot and shoulder.

The total number of children represented in this series is 112, 58 boys and 54 girls. Fifteen children appear in four yearly age groups; thirty-two in three, and twenty in two, but separate averages of traits for these children compared with those appearing for the first time in a group showed differences too slight to suggest overweighting by an element consistently large or small. Naturally, although roentgenograms were taken at intervals of three months for the plotting of individual growth curves, in the yearly divisions here presented, a child appears only once, at the age nearest the midpoint of the group.

To increase the number of cases in the first three years and to secure longer records on individual children, supplementary data have been gathered during the past year by the measurement of candidates for the Nursery School and for Group 3, younger brothers and sisters of children from the City and Country School, and others of a similar social background. Also, during this time roentgenograms and measurements have been made of children 7 and 8 years of age studied previously who are now outside the age limit of the Bureau's main interest.

The racial and environmental factors represented in the series are typical of a private school in a large American city. The physical and social environment is fairly uniform; the majority of the homes are in

* Received for publication, July 19, 1928.

the Chelsea or Greenwich Village sections of New York; moderate prosperity rather than wealth characterizes the background; all children from Group 5 upward lunch daily at the school, and only a few cannot receive a suitable diet throughout the year. Racially, the children represent old American stock,[1] other European strains of earlier or later importation, a mixture of these two, about 14 per cent of Jewish lines of varying European origin, and an additional 10 per cent of the last intermarried with the first three types. At the early ages here considered, the factors of growth and of nutrition so far outweigh possible racial differences—judging by the low variability of bodily proportions to be published later—that one would be justified in selecting sex and age as the only criteria for groupings, even without corroborative evidence from the development of the hand furnished by similar or different racial and social groups. Material available for comparison with the records of the City and Country School consists of roentgenograms of the hand, records of the stature and weight, for forty-four children of 5 and 6 years of age, from the Horace Mann School; similar data for 133 boys and 102 girls in the lower grades of a public school in Cleveland; and a series of twenty-eight Sicilian infants from the lower East Side of New York.[2]

SURVEY OF STUDIES OF THE HAND

It is not strange that in the thirty-three years since the discovery of the roentgen ray it should have been applied most often to the human wrist. The ease with which roentgenograms of the wrist can be made successfully, and the multiplicity of centers of ossification, present in early life, made it peculiarly adapted to practical and speculative purposes. Surgeons thus obtained a clear picture of a joint frequently

1. Hrdlička, Aleš: The Old Americans, Baltimore, 1925, p. 4.

2. The opportunity to analyze this divergent material and to discover therein certain general trends and relationships of skeletal growth and differentiation was given by Mrs. Lucy Sprague Mitchell and the Executive Committee of the Bureau of Educational Experiments, who granted both freedom of choice for the problem and every facility to carry it through. Miss Estelle Fine, statistician of the Bureau, advised in the work. Dr. Ramsay Spillman cooperated in taking and reading of the roentgenograms; Miss Lois Mills checked my records, and Miss Veda Elvin assisted in building up the younger age groups to visible size.

Prof. Arthur I. Gates of Teachers' College, Columbia University, and Mrs. J. R. McCastline, made possible the inclusion of the material in this study from the Horace Mann School. Mr. John C. Gebhardt offered the data on Sicilian infants. The large and important series of children from a Cleveland public school was made available by Dr. T. Wingate Todd, professor of anatomy in the School of Medicine, Western Reserve University; he also placed at my disposal the facilities of his laboratory and the wealth of his knowledge.

This problem was undertaken and carried out through the inspiration of Prof. Franz Boas.

fractured. From the changes in the distal portions of the diaphyses of radius and ulna, pediatricians could diagnose the presence and stage of rickets, and the great variability in size and number of centers for the carpal bones—the quality which in the present study points to their relative insignificance in the development of the child—seemed to offer to psychologists an individual physiologic index to relate with mental age.

The pioneer study of joints by roentgen-ray pictures, that of Poland, dealt exclusively with the wrist and hand.[3] Then in 1905 and 1908, Pryor and Rotch began their long series of publications devoted to the ossification and development of the wrist and the grading of roentgenograms. Both men used the method of inspection alone, but whereas Rotch [4] eliminated age and sex and classified roentgenograms only on the basis of carpal development with the heads of metacarpals and phalanges as controls in three of his thirteen groups, Pryor [5] continually emphasized the marked acceleration of the female in the development of centers for the carpus and the epiphyses of the hand from appearance in the embryo to union with diaphyses after puberty. Among the studies based on these inspectional classifications may be cited Bardeen's,[6] following Pryor, and that of Long and Caldwell [7] after Rotch. Long and Caldwell, working with clinic material, graded 200 roentgenograms ranging from those of infants to young men, and from idiots and cretins to the exceptionally bright high school boy. The results disappointed them; no easy way of sorting out the mentally and physically inferior was provided by a glance at the wrist alone. However, they concluded that in connection with such other factors as "sex, race, heredity, height and weight, it might serve as an aid to indicate the rapidity of skeletal development and possible future height of the child." An interesting sidelight on the errors of the inspectional method is found in the statement that there are "so many discrepancies in development between the right and the left wrist of the same individual that we must doubt the value of using a roentgenogram of the wrist as an accurate

3. Cohn, Isadore: Normal Bones and Joints Roentgenologically Considered, Ann. Roentgenol. **4**:2, 1924.

4. Rotch, T. M.: The Roentgen Ray in Pediatrics: Living Anatomy and Pathology. The Diagnosis of Diseases in Early Life by the Roentgen Method, Philadelphia, 1910, p. 54, table 4.

5. Pryor, J. W.: Time of Ossification of Bones of the Hand in the Male and Female and Union of Epiphyses with the Diaphyses, Am. J. Physical Anthropology **8**:401, 1925.

6. Bardeen, C. P.: The Relation of Ossification to Physiological Development, J. Radiol. **2**:1, 1921.

7. Long, Eli, and Caldwell, E. W.: Some Investigations Concerning the Relation Between Carpal Ossification and Physical and Mental Development, Am. J. Dis. Child. **1**:113 (Feb.) 1911.

index of the development of any other part of the body." This is in striking contrast to the observations of Stettner [8] and Baldwin,[9] who stated that average differences are so slight that in their studies of the appearance of centers and of the area of carpal bones, they have used only one hand, the right. Todd confines his investigations to the left hand. For the groups of children from the City and Country School, the average differences have been calculated in all sex and age groups (tables 6, 10, 12), and the results agree, for all practical purposes, with the latter opinion.

When Bardeen [6] separated the roentgenograms of 167 Wisconsin school children, ranging from 3 years, 5 months to 13 years, 5 months of age, into eleven stages based on the number of carpal centers, their density and size (after the inspectional method of Pryor), and related these to the height and weight, he concluded that ossification was unsatisfactory as a practical method of judging general physiologic development. The main reason he puts forth is that relationship between retardation and acceleration in stature and ossification of the wrist was usually slight, whereas a close relationship existed between stature and weight, disregarding the degree to which two measurements so mutually conclusive as height and weight must necessarily yield a spurious correlation.

Far in advance in method, statistical treatment and scientific point of view is Baldwin's [9] study of the growth in the exposed carpal area in twenty-three boys and thirty-one girls, over a period of three years, the ages from beginning to end ranging from 8 to 13 years. The sum of the areas of each of the carpal bones, as determined by planimeter tracing, yielded the results indicated by Pryor and supported by subsequent studies of different sections of the hand by various methods: (1) girls at a given chronologic age have a much greater exposed surface area of carpal bones than have boys, and (2) in this character boys are much more variable than girls. High positive correlations were obtained between the carpal areas and height and weight. Since the publication of these observations in 1921, numerous psychologists have made wide use of the method as a means of correlating the so-called anatomic age with the mental age established by intelligence tests. It is not my purpose to discuss their conclusions and the general results of comparisons of mental and physical traits. A representative list of such studies from

8. Stettner, Ernst: Ueber die Beziehungen der Ossifikation des Handskeletts zu Alter und Längenwachstum bei gesunden und kranken Kindern von der Geburt bis zur Pubertät, Arch. f. Kinderh. **68**:342 and 439, 1920-1921; **69**:27, 1921; **70**: 62, 1922.

9. Baldwin, B. T.: The Physical Growth of Children from Birth to Maturity, University of Iowa Studies in Child Welfare **1**:167, 1921.

1893 to 1923 has been published by Gates.[10] To various of these investigators, Baldwin's statement of the gross carpal area lacked the significance to be found in the possible expression of ossification present to the area of final ossification. Gates [11] and Freeman and Carter [12] attempted solution by computing the area of the quadrilateral formed by joining the points "placed on the extreme outer corners of the first metacarpal, fifth metacarpal, the ulna and the radius." Prescott,[13] on the contrary, does not use the quadrilateral, but instead the sum of the diameters of the carpal bones divided by a diameter drawn from the most external point of the base of the metacarpal bone of the thumb to the internal point where the base of the fifth metacarpal bone touches the fourth. This anatomic index he defends on the basis of its high correlation with the subjective ranking of the same roentgenograms. As correlations with other physical traits are not attempted, Prescott's only observations suggestive to this study are a repetition of Baldwin's [9] results, acceleration of girls over boys and greater variability of boys, with the addition of high individual variability in both sexes.

Gates, however, correlated the area and ratio of ossification with eight other physical traits, the coefficients being low except with height and weight, which, while lower than Baldwin's, were definitely significant.

Objections to studies of the types just cited are of several varieties. The purely technical point is raised by Scammon—the extreme error in the polar planimeter used by all these men, owing to the personal equation involved in the direction of the tracing point, an error particularly present with small areas. Prescott substituted for this error the results of tracings from a projectoscope which enlarged the film 5 diameters. Scammon [14] himself suggests the calculation of area by weight of tracings cut from celluloid.

It seems more fundamental, however, to question the significance of the size and development of the carpus and the constancy of its value

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10. Gates, A. I., and others: The Educational Significance of Physical Status and of Mental, Physiological, Social and Emotional Maturity, J. Ed. Psych. **15**: 332, 1924.

11. Gates, A. I., and others: The Educational Significance of Physical Status and of Physiological, Mental, Emotional and Social Maturity, Teachers College Record **25**:223, 1924.

12. Freeman, F. N., and Carter, T. M.: A New Measure of the Development of the Carpal Bones and Its Relation to Physical and Mental Development, J. Ed. Psych. **15**:257, 1924.

13. Prescott, D. A.: The Determination of Anatomical Age in School Children and Its Relation to Mental Development, Harvard Monographs in Education **5**: 1 (July) 1923.

14. Scammon, R. E., and Scott, G. H.: The Technique of Determining Irregular Areas in Morphological Studies, Anat. Record **35**:269, 1927.

for all ages considered in these investigations. While it is probable that after 7 years of age—the age at which Baldwin's series begin and the end-point of my groups—there is growth and extensive differentiation of the carpal bones, not mere spread of ossification, it is doubtful if the high correlations here found with height and weight would extend from 6 months to 6 years of age. Many of Prescott's school children are 5 and 6 years old, and Gates' younger group with a mean age of 5½ has an age range of from 2 years, 8 months to 6 years, 5 months. For my series, from 6 months through 7 years, as will be demonstrated later, in the relationships with stature, weight, size of diaphysis and general medical observations, the ossification of carpal centers is of little significance beside the part played by the epiphyses for the radius and for the bones of the hand and fingers.

A study of a different sort, in which the hand as a whole is considered, is Stettner's [8] classification of 700 roentgenograms of children from the clinic of Erlangen University. Only the 250 normal cases are considered here, that is, children with neither chronic illness nor rachitic symptoms. They represent an ethnic unit remarkably pure. To the enumeration of centers for epiphyses of the radius, ulna, hand and fingers, and the centers of carpal bones for each age and sex are added measurements of stature. Unfortunately, considering the small number of children and the long range from birth to puberty, Stettner first divided the children into three social classes—*Grossbürgerskinder*, workmen's children from Erlangen, and country children from the suburbs—and subdivided each sex and social group into three according to stature. While his conclusions are that degrees of ossification follow each other in a regular progression from short country children to tall city children of prosperous parents, the frequencies in these groups of from one to twenty-two cases and their age ranges from 4 weeks to 13 years rob them for the present of significance. Two groups, however, are of reasonable size, those of workmen's children of medium stature, which include fifty-seven boys and sixty-eight girls. On these, Stettner based his graphs for the number of centers in relation to age and stature. Unfortunately, however, these tables with their ranges of 14 days to 13 years, 6 months and 10 days to 12 years, respectively, have been copied by Bürger and Schecht,[15] and have been used extensively by pediatricians, who, through no fault of Stettner's, believe them to be based on his entire 700 cases. Another scale produced in Germany at about the same time is the Normaltafeln of St. Engel and Runge [16] which, while stressing the enormous individual variations in

15. Bürger and Schecht: Lehrbuch der Röntgendiagnostik, 1924, vol. 2, p. 1167.

16. St. Engel and Runge: Normaltafeln des Kindesalters, Ztschr. f. Kinderh. **33**:61, 1922.

the appearance of epiphyses and centers, takes no account of the equally important sex differences.

Within the last year, Stettner's valuable, if insufficient material, has been further developed by Munk,[17] one of his students, who on a series of 300 normal children in a clinic—probably in the main the normal series of Stettner—has measured the anteroposterior and transverse diameters of carpals and epiphyses appearing on these plates. Reference will be made later to the means thus obtained.

More fundamental from the biologic standpoint than any of the foregoing studies is the attempt of Prof. T. Wingate Todd [18] to extend his masterly survey of the age changes in the adult skeleton to roentgenograms of the joints of school children. Since few children in his series are under 6 years of age, his qualitative scale does not reach the majority of my groups, so while it is my purpose later to develop, if possible, a similar system for the ages from 2 through 5 and then to apply Todd's standards to the older groups, it does not lie within the scope of the present paper. It may be interesting to note, however, that working independently and from widely different points of view, both Dr. Todd and I selected the distal epiphysis of the radius, and the metacarpals and phalanges as the most promising portions of the hand in which to solve the separate problems of the uniformity of differentiation, and of the extent of normal variability in quantitative traits.

Of great significance in this matter of the development of the phalanges, although at the opposite end of the age scale to this study, is the paper just published by Hellman [19] on the ossification of the hands of sixty girls from 10 to 15 years of age in the Hebrew Orphan Asylum of New York. Dr. Hellman followed individuals over a period of four years, recording annual increments for each metacarpal and phalanx, and noting the sequence of ossification of epiphyses. Further mention will be made of the order of union. It was found that the average age of the greatest increment of growth of bone preceded the greatest growth in stature by one year.

The review of the long series of articles from which the foregoing were selected shows an almost complete dearth of material dealing with the ossification of the normal, nonclinical child, considering this process either alone or in relation to other physical traits, and little on

17. Munk, A.: Die Kerngrössen der Handwurzelknochen und des distalem Unterarmabschnittes bei normalwuchsigen Kindern von der Geburt bis zur Pubertät, Arch. f. Kinderh. **80**:185, 1927.

18. Todd, T. W.: The Radiographic Study of Skeletal Growth in Children, read before the Galton Society, New York, 1927.

19. Hellman, Milo: Ossification of Epiphysial Cartilages in the Hand, Am. J. Phys. Anthrop. **11**:223, 1928.

older children that is not open to question from the point of view of biologic significance. I do not hesitate, therefore, to present a tentative study of groups no larger than those at present collected by the Bureau of Educational Experiments, trusting that the near future will bring forth investigations more conclusive both here and elsewhere.

PHYSICAL STATUS OF CHILDREN IN THE STUDY

At all ages the children from the City and Country School, with whom this study is primarily concerned, present the high averages for

TABLE 1.—*Stature and Weight of Children in Study of Growth and Ossification of the Hand*

	City and Country School					Cleveland Public School*			Horace Mann School				
	Length, Cm.		Weight, Kg.			Height, Cm.	Weight, Kg.		Height, Cm.		Weight, Kg.		
Age, Year	Mean	Standard Deviation	Mean	Standard Deviation	f	Mean	Mean	f	Mean	Standard Deviation	Mean	Standard Deviation	f
						Boys							
1†	76.0	5.80	10.4	1.66	10	.....	....	..	.....	. ..	....	....	..
2	91.1	2.89	13.6	1.23	11	.....	....	..	.....	. .	....	....	..
3	97.0	4.50	14.9	1.46	16	.....	....	.	.... .	....	....	....	..
4	104.0	4.30	16.8	1.62	21	.....	....	..	.....	....	....	....	..
5	110.9	5.20	18.8	2.17	22	.....	....	..	109.6	4.75	18.7	2.14	16
6	116.7	3.65	20.5	1.80	20	111.5	20.0	16	110.9	4.17	19.5	1.96	8
7	124.6	5.63	23.7	3.38	11	118.6	23.1	29	.... .	....	....	....	..
8	128.0	5.25	25.2	3.92	9	123.8	25.4	39	. ...	....	....	....	..
						Girls							
1†	75.2	3.17	10.7	1.24	7	.....	....	..	.....	...	....	....	..
2	87.2	3.44	12.1	1.23	11	.....	....	.	.....	. ..	....	.. .	..
3	95.7	5.34	14.7	1.47	14	.... .	....	..	....	....	....	....	..
4	103.6	2.47	17.1	1.67	24	.....	....	..	.....	....	....	....	.
5	110.6	4.78	18.9	1.76	24	.....	....	..	108.7	3.60	18.4	1.75	15
6	115.9	4.03	21.0	1.89	21	112.3	20.0	16	115.0	2.52	20.4	1.57	9
7	122.6	4.88	23.5	2.10	15	118.2	21.8	23	.....	....	....	....	..
8	132.5	....	27.9	....	5	124.2	24.5	26	.....	....	....	....	..

* A sample group of the children in the study of growth and ossification of the radius. All heights and weights taken while children in this group were fully clothed.
† Means and standard deviations for one year of very slight significance because of long age range during period of rapid growth.

stature and weight to be expected in a private school (table 1). Abundant evidence for increased averages for height and weight with financial prosperity has been offered by Boas'[20] means for differences in these traits as recorded in an orphanage, a public and a private school, and by the numerous German studies from a variety of social strata.[21] Group medians for boys from such schools as Groton, Middlesex and Hill, and for girls from Chicago private schools[22] present

20. Boas, Franz: The Growth of Children as Influenced by Environmental and Hereditary Conditions, School and Society **17**:305, 1923.

21. Schlesinger, Eugen: Das Wachstum des Kindes, Berlin, 1926, p. 63.

22. Gray, H., and Fraley, F.: Growth Standards for Private School Boys, Am. J. Dis. Child. **32**:554 (Oct.) 1926. Gray, Horace, and Gower, Charlotte: Growth Standards of Height and Weight for Girls in Private Schools, ibid. **35**:411 (March) 1928.

consistent proof of this, the boys and girls being always taller and heavier than the group of gifted California children whom Baldwin found above the best standards for the American born.[23]

Of the children in the comparative series, those of the Horace Mann School do not show any differences that cannot be explained by the smallness of the sample. The measurements from the Cleveland public school, on the other hand—unfortunately only a sample of the groups used in the study of ossification—show the small stature resulting from poorer average nutrition and a considerable percentage of Sicilian stock. This is the more striking when one considers that height standing was taken with shoes included. As weights were taken with the children fully clothed, they will not be discussed. The Sicilian infants, from the lower East Side of New York, show the same differences in relation to a group of eight boys from the Bureau Nursery School, with individual measurements selected at ages younger than those used in the one year group (table 5). The length of the boys from the Nursery

TABLE 2.—*Comparative Stature of Girls 7 Years of Age*

Group	Mean Stature	Frequency
City and Country school	122.6	15
Chicago private schools	123.4 (median)	58
California gifted children	120.9	13
Cleveland public schools	118.2 (with shoes)	23

School at an average age of 10.5 months is 74.1 ± 5.5 cm.; of fourteen Sicilian boys (9.1 months) 68.3 ± 4.0; weight, boys from the Nursery School, 9.9 ± 1.7 Kg.; Sicilian, 8.2 ± 1.2. A picture of the relative stature of the children with whom this study is concerned, in relation to standards above the usual averages, is given in table 2 as it occurs among girls 7 years of age.

The stature of all children in the series from the Bureau through 6 years and some in the 7 year group, is measured in the reclining position, which for young children gives an increase of from 0.5 to 2.5 cm. over height standing, subject to wide individual variation within each age limit. Only the weights of nude children are recorded. All weights and statures, part of the detailed anthropometric measurements, taken bimonthly, are never more than one month distant from the date of the roentgenogram. Both measurements and roentgenograms have been selected nearest the mid-point of each year group, without regard for seasonal variation. Figures based on the three years, from 1925 to 1927, show that whatever climatic influence may exist is entirely obscured by the home environment.

23. Anthropometric Measurements of Gifted Children, reprinted from Genetic Studies of Genius, Stanford University Press, 1925, vol. 1.

In spite of the seasonal fluctuation in the calcium content of the blood stream noted by Bakwin,[24] the majority of carpal centers, the appearance of which could be definitely recorded as "first," fell into no consistently significant time of the year.

Unfortunately, the material is at present insufficient to prove whether children born in the spring have, over a period of years, a higher average for stature, weight and ossification than children born in the supposedly less advantageous autumn.

TABLE 3.—*Average Seasonal Gains in Stature and Weight, 1925-1927*

	Stature, Cm.	Weight, Kg.	Frequency
Boys			
November-May	3.7 ± 1.2	0.97 ± 0.49	57
May-November	3.5 ± 1.35	0.98 ± 0.57	55
Girls			
November-May	3.6 ± 0.41	1.2 ± 0.63	61
May-November	3.4 ± 0.92	0.99 ± 0.56	52

TABLE 4.—*Carpal Centers—Time of Appearance*

	November to May	May to November	August to November	November to February	February to May
Boys	47	57	41	25	20
Girls	72	68	39	32	45

TABLE 5.—*Average Ages, City and Country School*

	Year	Boys	Girls
12 months	1	11.6	12.4
24 months	2	25.7	24.0
36 months	3	35.8	35.4
48 months	4	47.3	47.8
60 months	5	59.6	60.0
72 months	6	71.0	71.1
84 months	7	83.5	83.5
96 months	8	94.1	96.6

Grouping of Material.—All records of stature, weight, dentition and development of the hand are arranged by sex, in sixteen yearly groups of from 1 to 8 years of age. 1 year=0 years, 6 months to 1 year, 5 months, etc. The roentgenogram of each child is selected nearest to 1 year, 2 years, and so on, and the observations correlated with the stature, weight and dental record fall within a month of that date.

It is interesting to note that in the younger groups, in which the acceleration of ossification in girls over boys is particularly marked, the boys are older than the girls.

Records of the Horace Mann and Cleveland schools and of the Sicilians are arranged by the same system.

24. Bakwin, Harry, and Bakwin, R. M.: Seasonal Variation in the Calcium Content of Infants' Serum, Am. J. Dis. Child. **34**:994 (Dec.) 1927.

OSSIFICATION AND GROWTH OF THE HAND

An extended survey of the roentgenograms of the hand, with the intention of selecting certain characters common to all ages which might be linked with such other physiologic factors as stature, weight and eruption of teeth, strongly suggested two conclusions which this completed study seems to substantiate: (1) the erratic character of early ossification in carpal centers, and (2) the more orderly and relevant development of the epiphyses for the metacarpals, phalanges and the distal extremities of the radius and ulna. This statement is most strikingly illustrated in the children from the City and Country School from 2 to 4 years of age, who are known to have suffered from early malnutrition. Carpal centers often appear of a size and number above the average, but the epiphysis for the radius is small in relation to its diaphysis, and between the metacarpals and the rows of phalanges, there are a remarkable number of gaps. One boy, 15 months of age, who showed healing rickets and was therefore excluded from the study, had four carpal centers, the mean for boys of 5 years, but not a single epiphysis for the bones of the hand and fingers.

These observations coupled with the statement of an anatomist of the standing of Dr. Todd that "the time of commencing 'precipitation' of bone in the wrist cartilages is erratic," and added to the technical errors involved in the measurement of small irregular areas, led to the decision to direct greater effort to the study of the epiphyses. The carpal centers, however, have not been overlooked. Their presence and time of appearance have been noted for each group, and the numbers have been correlated with all the other selected factors of growth. The fact that the values of these coefficients of correlation are lower than the *r's* for the same traits with number of epiphyses for metacarpals and phalanges, seem clearly to justify this subordination. In general, there is some relationship between carpal bones and other areas of spreading ossification, but almost none with growth of bone or with the height and weight.

The epiphyses of the hand and wrist available for study were: (1) the nineteen centers for metacarpals and phalanges, evidently significant, but only for the earliest years of this series; (2) the epiphysis of the ulna, which rarely appears before 5 years of age, which is most irregular throughout the 8 year group, and which does not enter directly into the articulation and function of the wrist; (3) the epiphysis of the radius. The last, present in all but four films used in the series, shows steady development and consistent age and sex differences from 1 to 8 years. It provides, in the approach of its maximum transverse diameter to that of the diaphysis, an excellent index of spread of ossification to growth of bone; and, since the ratio does

not reach 100 until after the age of 8 years, it is of significance throughout the period. As will be seen later, the correlations of this index and of the two diameters involved, with centers of ossification and with the gross bodily size, offer the most striking points of interest in the present study.

Before arriving at these interrelationships, however, it is necessary to set forth quantitative differences brought about by age, sex and

TABLE 6.—*Growth and Ossification of the Carpus, Number of Centers*

	City and Country School						Cleveland Public School			Horace Mann School		
	Right Hand			Left Hand			Left Hand			Right Hand		
Age	Mean	Standard Deviation	f	Mean	Standard Deviation	f	Mean	Standard Deviation	f	Mean	Standard Deviation	f
						Boys						
1 year	2.2	0.40	10	...	....	..	...	....	..	...	....	..
2 years	2.6	0.64	11	2.6	0.66	10	...	....	..	...	....	..
3 years	3.3	1.10	16	3.3	1.09	16	...	....	..	...	....	..
4 years	3.4	1.33	21	3.4	1.29	21	...	....	..	...	....	..
5 years	4.2	1.38	22	4.1	1.35	22	4.6	1.04	9	4.4	1.49	16
6 years	4.8	1.50	20	4.7	1.49	20	5.2	1.35	40	5.0	1.58	8
7 years	6.4	1.37	11	6.3	1.35	11	6.3	0.96	40	...	....	..
8 years	6.7	0.94	9	6.7	0.67	9	6.8	0.61	44	...	....	..
						Girls						
1 year	2.1	0.35	7	...	....	..	...	....	..	...	....	..
2 years	3.0	0.95	11	3.0	0.89	10	...	....	..	...	....	..
3 years	3.4	1.29	14	3.5	1.28	13	...	....	..	...	....	..
4 years	5.4	1.53	24	5.2	1.58	24	...	....	..	...	....	..
5 years	6.3	0.90	24	6.1	1.05	24	7.0	0.00	9	6.5	0.78	11
6 years	6.9	0.29	21	6.9	0.43	21	6.6	0.70	31	7.0	0.00	9
7 years	7.1	0.25	15	7.0	0.37	15	6.9	0.55	32	...	....	..
8 years	7.4	....	5	7.4	....	5	7.0	0.00	30	...	....	..

TABLE 7.—*City and Country School, Ossification of Carpal Centers, Percentage Present at Each Age*

Age	1 Year		2 Years		3 Years		4 Years		5 Years		6 Years		7 Years		8 Years	
	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀
Carpal centers																
Cuneiform	20	29	60	64	82	88	75	100	88	100	100	100	100	100	100	100
Semilunar	00	00	20	27	29	63	50	88	72	100	86	100	100	100	100	100
Trapezium	00	00	00	18	12	25	13	68	28	93	50	96	81	100	100	100
Trapezoid	00	00	00	00	00	00	8	64	16	81	38	100	81	100	89	100
Scaphoid	00	00	00	00	12	7	21	56	24	93	48	100	81	100	89	100
Distal epiphysis																
Ulna	00	00	00	00	00	00	00	16	16	37	29	60	56	94	67	100
Frequencies	10	7	15	11	17	16	24	25	25	27	22	25	16	17	9	9

environment in the carpus, the epiphyses and the diaphysis of the radius, and their separate variabilities.

Carpus.—The centers of ossification for the eight bones of the wrist, although not so vitally connected with the young child's growth as are other features in the hand, offer a clear picture of the retardation of the boys. The higher degree of variability for boys than for girls through-

out their early development is due to their slower approach to a final variability of zero. These sex differences in amount and time of ossification are presented by three methods in tables 6, 7, 8 and 9.

From table 6 on which the average number of bones present in each group has been calculated together with the mean square deviations, these facts are immediately apparent: the greater number of bones present in girls at all ages from 4 through 8 years and the close

TABLE 8.—*First Appearance of Carpal Centers, Mean Age and Range*

	City and Country School						Davies and Parsons*
	Boys			Girls			
Carpal centers	Mean	Range†	f	Mean	Range†	f	Range‡
Cuneiform....	3 yr., 1 mo.	0 yr., 9 mo. to 5 yr., 7 mo.	14	2 yr., 1 mo.	1 yr., 2 mo. to 3 yr., 1 mo.	8	2 years to 4 years
Semilunar.....	4 yr., 5 mo.	1 yr., 4 mo. to 6 yr., 6 mo.	17	3 yr., 8 mo.	2 yr., 0 mo. to 4 yr., 6 mo.	11	3 years to 4 years
Trapezium....	5 yr., 9 mo.	3 yr., 2 mo. to 7 yr., 8 mo.	11	4 yr., 7 mo.	1 yr., 11 mo. to 7 yr., 0 mo.	18	6 years to 7 years
Trapezoid.....	6 yr., 0 mo.	3 yr., 6 mo. to 7 yr., 10 mo.	10	4 yr., 8 mo.	3 yr., 2 mo. to 6 yr., 1 mo.	11	7 years to 8 years
Scaphoid.....	5 yr., 4 mo.	3 yr., 2 mo. to 7 yr., 10 mo.	9	4 yr., 9 mo.	3 yr., 2 mo. to 6 yr., 8 mo.	21	6 years to 8 years
Distal epiphysis Ulna.....	5 yr., 10 mo.	4 yr., 11 mo. to 8 yr., 3 mo.	11	5 yr., 3 mo.	4 yr., 1 mo. to 8 yr., 5 mo.	23	7 years to 8 years

* Sexes undifferentiated.
† Earliest age present to last age absent.
‡ Range in which greatest frequency occurs.

TABLE 9.—*First Appearance of Carpal Centers Derived from Table 7*

	Boys		Girls	
	Mean	Standard Deviations	Mean	Standard Deviations
Cuneiform.....	1 year, 8 months	2.67	1 year, 7 months	1.15
Semilunar.....	3 years, 11 months	1.98	2 years, 8 months	1.12
Trapezium.....	5 years, 11 months	1.85	3 years, 6 months	1.14
Trapezoid.....	6 years, 2 months	1.32	3 years, 4 months	1.93
Scaphoid.....	5 years, 11 months	2.03	3 years, 11 months	0.75
Ulna.....	6 years, 11 months	1.92	5 years, 7 months	1.59

approximation of means for the City and Country School with the Horace Mann School and with the socially and racially diverse group from Cleveland. The average number of carpal centers for the New York Sicilian infants (fourteen boys, average age 9.1 months, fourteen girls, 8.1 months) are 2.3 ± 0.42 and 2.2 ± 0.56, while the average for eight boys of the Nursery School calculated from the youngest age at which roentgenograms were taken rather than that nearest the mean (10.5 rather than 11.6) is 2.3 ± 0.44. The general uniformity of these results points to two things: (1) the slight variation in the number of

carpal bones present in groups of normal children of the same age and sex as opposed to the high variability in individuals, and (2) the apparent reliability of the small sample represented by the City and Country School compared with the Cleveland groups of twice the size. It is evident that in number of centers, there is no real difference between the right and the left hand. Observation of the long series of plates establishes the fact that in the rare case in which first appearance is asymmetrical, the second center usually commences ossification within the next three months.

The percentage of the carpal bones,[25] as well as the distal epiphyses for the radius and ulna present in children from the City and Country School from 1 to 8 years of age, is recorded in table 7. For most centers, the boys reach 100 per cent at least two years after the girls. Scammon's table [26] would doubtless give corresponding age percentages if the sexes were separated.

The third presentation of carpal ossification (table 8) is a record of the actual first appearance of centers. Only those centers are included which were not visible on the plate of the same child three months earlier. From the time when the center was first seen, one and one-half months was subtracted, thus giving an age halfway between the last observation of absence and the first observation of appearance. By this method also, the girls lead the boys in the age of appearance for each carpal center. Still more striking is the greater range for recorded first appearance of any center in the male carpus. Beside these results are the figures of Davies and Parsons,[27] who place the ages of ossification earlier than in the majority of textbooks. Although they are aware of female acceleration, sex differences are not stated in their final averages.

At the suggestion of Professor Boas, a further attempt to determine the age of first appearance was made by fitting the figures of table 7 to the probability curve, the method which he described and applied in *Statistics of Growth* [28] (table 9).

The differences between these theoretical averages and the actual appearance recorded in table 8 rise partly from the inevitable inaccuracies of the method, but on the other hand, when the age is less than in table 8, it may well be a truer picture, since, for certain bones, many of the more advanced children enter the school already in possession of

25. Os magnum and unciform was present in all City and Country Children; pisiform in 1 girl, aged 7 years, and in 2 girls, aged 8 years.

26. Outline of Anatomy. After Puyhaubert, 1913, and Adair and Scammon, 1921.

27. Davies, D. A., and Parsons, F. G.: The Age Order of the Appearance and Union of the Normal Epiphyses as Seen in X-Rays, J. Anat. **62**:58, 1927.

28. Boas, Franz, and Wissler, Clark: Statistics of Growth, Report of Commissioner, U. S. Bureau of Education for 1904, **2**:25, 1904.

centers, the first appearance of which is therefore noted only in retarded children. All age groups show the same sex difference in rate characteristic of other parts of this study.

The distal epiphysis of the ulna will be discussed in a later section.

The order in which the centers for the first seven bones of the carpus make their appearance is well known, and a restatement of small disputes over the sequence of the last three of these can hardly be valuable or exciting. Therefore, the following statements are based on descriptions of the Bureau's series alone.

With one exception, the first three bones to appear in the wrists of sixteen boys and twenty-three girls were: the os magnum, the unciform, the cuneiform. In the exception, a boy, the third was the semilunar.

In all but three cases (girls), the fourth bone to appear was the semilunar. In one of the exceptions, the trapezoid was the fourth bone to appear and the semilunar, the fifth. In another, the trapezium appeared fourth and the scaphoid fifth; the semilunar was still absent at 3 years, 10 months of age. In the third, the trapezium appeared fourth, the trapezoid fifth, and the semilunar sixth.

The first in order of appearance of the trapezium, trapezoid and scaphoid as recorded for 35 subjects, was the trapezium in 18 cases, the trapezoid in 8, the scaphoid in 9. Of 21 cases, the last to appear was the trapezium in 7 instances, the trapezoid in 9 and the scaphoid in 5. The interval between the appearance of the first and the last of these three bones noted in 13 children was: three boys, 9, 10, and 28 months, respectively; ten girls, mean interval 8.4 months, range 3 to 14 months.

Radius—Distal Epiphysis.—The epiphysis for the lower extremity of the radius is present in all but four children in the groups from the City and Country School; namely, two boys of 6 and 10 months, and one girl of 11 months in the 1 year groups, and a boy 2 years and 4 months. It was present, however, in a girl of 10 months the youngest in the group, and in a boy of 10 months, the diameter (7 mm.) pointing to an appearance some months earlier. Of the twenty-eight Sicilian infants, the youngest with this epiphysis were a girl of 7 months and a boy of 8 months; the oldest lacking it were (girl) 11 and (boy) 14 months.

The figures for the maximum transverse diameter of the epiphyses which appear in tables 10, 11 and 13 were obtained with a Colin sliding caliper, directly from the films. Measurements were read to the nearest millimeter for both this and the diameter of the diaphysis, the indistinctness of some plates making greater accuracy unprofitable. All roentgenograms were made at a uniform distance (36 inches) from the

subject whose wrist and hand lay flat on the plate. Davies and Parsons [27] note that the actual size of the bone can never be more than the measurement, though sometimes it may be a little less. This study is not concerned with the actual size of epiphysis and diaphysis in the roentgenogram and the living child, but with the relationship of these two factors as seen in the plate, which there is no reason to doubt corresponds to the same degrees of growth and ossification in the children. Moreover, many children had nine plates each, covering a period of three years, and the measurements of these plates, taken with the name and

TABLE 10.—*Growth and Ossification of the Radius (Distal Extremity), Epiphysis (Maximum Transverse Diameter)*

	City and Country School									Cleveland Public School			Horace Mann School		
	Right Hand			Left Hand			Difference Right — Left			Left Hand			Right Hand		
Age	Mean	Standard Deviation	f	Mean	Standard Deviation	f	Mean	Standard Deviation	f	Mean	Standard Deviation	f	Mean	Standard Deviation	f
Boys															
1 year	2.8	2.48	10	....	....	..	.....	....	..	....	....	..	....	....	..
2 years	7.3	4.18	11	7.0	3.26	10	—0.6	1.02	10	....	..	..	....	....	..
3 years	10.8	3.09	16	11.7	2.54	16	—0.9	1.09	16	....	....	..	....	....	..
4 years	12.5	3.13	21	13.5	2.69	20	—1.0	1.18	20	....	....	..	....	....	..
5 years	15.4	2.79	22	15.8	2.48	22	—0.4	0.98	22	16.3	1.89	9	16.4	2.32	16
6 years	17.5	2.36	20	17.6	2.37	20	—0.1	0.62	20	17.8	1.68	40	16.8	2.17	8
7 years	20.8	1.90	11	21.0	2.17	11	—0.2	0.72	11	19.7	1.89	40	....	....	..
8 years	21.7	1.83	9	22.4	1.95	9	—0.8	1.03	9	21.4	1.86	44	....	....	..
Girls															
1 year	3.9	3.65	7	....	....	..	.....	....	..	....	....	..	....	....	..
2 years	9.0	1.86	11	9.5	2.01	10	—0.6	0.92	10	....	....	..	....	....	..
3 years	12.3	2.02	14	12.2	2.39	13	—0.5	0.64	13	....	....	..	....	....	..
4 years	14.7	1.64	24	15.3	1.86	24	—0.5	0.82	24	....	....	..	....	....	..
5 years	17.1	1.75	24	17.5	1.83	24	—0.4	0.86	24	16.8	1.87	9	16.7	1.81	11
6 years	18.6	1.59	21	18.9	1.64	21	—0.2	0.68	21	17.5	1.60	31	19.2	1.13	9
7 years	20.5	1.89	15	20.6	1.74	15	—0.1	0.50	15	19.2	2.13	32	....	....	..
8 years	23.6	....	5	23.6	....	5	0.0	....	5	21.5	1.95	30	....	....	..

age of the child not known to the observer, showed small, regular gains throughout the period, which fully justify the method. Table 10 shows the spread of ossification in the same groups as table 6. For the City and Country School, sex differences in acceleration and in variability are similar to the conditions for the number of carpal centers. Small average differences between the hands exist at all ages, consistently in favor of the left hand. Comparison with the means of the children from Cleveland should therefore be made from this hand. The small groups for 6 years from the Horace Mann School show the same relative variabilities as the groups from the City and Country School. The means of the Cleveland boys are always smaller, the variabilities lower and equal to those of the girls. The epiphyses of the girls, however, are smaller than in the children from the City and Country School, both absolutely and in relation to the boys, but their average variabilities are the same. The standard devia-

tions of the boys from the City and Country School, the most uniformly variable group, naturally decrease with age, being the same as the girls at 7, and matching the Cleveland boys at 8, when the diameter of the epiphysis nearly equals that of the diaphysis.

After four years, the rate of ossification is slower, the annual increment decreasing from 4 or 5 mm. to 2 mm. The same is true for the

TABLE 11.—*Radius (Diameter of Distal Epiphysis)*

	Girls	
	Erlangen Clinic	City and Country School
1 year	3.7	3.9
2 years	7.1	9.0
3 years	10.6	12.3
4 years	13.8	14.7
5 years	14.6	17.1
6 years	17.3	18.6
7 years	19.6	20.5
8 years	20.3	21.6

TABLE 12.—*Growth and Ossification of the Radius (Distal Extremity), Diaphysis (Maximum Transverse Diameter)*

	City and Country School									Cleveland Public School			Horace Mann School		
	Right Hand			Left Hand			Difference Right — Left			Left Hand			Right Hand		
Age	Mean	Standard Deviation	f	Mean	Standard Deviation	f	Mean	Standard Deviation	f	Mean	Standard Deviation	f	Mean	Standard Deviation	f
Boys															
1 year	15.6	1.02	10	....	....	..	.....	....	..	....	....	..	....	....	..
2 years	17.6	0.98	11	18.4	0.80	10	—0.8	0.75	10	....	....	..	....	....	..
3 years	18.1	0.78	16	19.1	0.97	16	—0.9	0.75	16	....	....	..	....	....	..
4 years	18.9	1.19	21	19.6	1.09	21	—0.7	0.64	21	....	....	..	....	....	..
5 years	20.0	1.37	22	20.8	1.61	22	—0.8	0.73	22	20.6	0.83	9	20.1	1.35	16
6 years	21.1	1.04	20	21.6	1.11	20	—0.5	0.81	20	21.3	1.46	40	20.3	0.97	8
7 years	22.7	1.76	11	23.2	1.47	11	—0.5	0.78	11	22.1	1.28	40	....	....	..
8 years	22.8	1.87	9	23.3	2.21	9	—0.6	0.69	9	22.8	1.67	44	....	....	..
Girls															
1 year	14.9	1.45	7	....	....	..	.....	....	..	....	....	..	....	....	..
2 years	16.2	1.03	11	17.1	0.83	10	—0.7	0.64	10	....	....	..	....	....	..
3 years	17.5	0.73	14	18.2	1.17	13	—0.6	0.84	13	....	....	..	....	....	..
4 years	18.6	1.00	24	19.3	1.07	24	—0.8	0.52	24	....	....	..	....	....	..
5 years	19.5	1.29	24	20.5	1.50	24	—0.9	0.64	24	18.8	1.13	9	18.8	1.27	11
6 years	20.5	1.26	21	20.9	1.32	21	—0.4	0.65	21	19.5	1.07	31	20.0	0.82	9
7 years	21.5	1.41	15	21.7	1.48	15	—0.3	0.68	15	20.7	1.45	32	....	....	..
8 years	23.0	....	5	23.0	....	5	0.0	....	5	21.6	1.96	30	....	....	..

girls studied by Munk.[17] His 6-month age groups have been combined in table 11. The number of cases is not stated. The right hand alone was used.

The consistently greater diameters for the girls from private schools, while perhaps in part caused by the lower averages in Munk's series where ages are not stated, more probably are due to the contrast between the normal children of an American private school and children from a German clinic during the spring and summer of 1918.

Radius—Diaphysis.—The growth of bone, as represented by the greatest transverse diameter of the distal end of the radial shaft, presents contrasting features highly significant in relation to the process of ossification. The average size for boys is always larger than that for girls. Compared with table 10, the standard deviations of table 12 are, consequently, lower and equal for boys and girls. Small steady gains in diameter of about 1 mm. a year for both sexes from 2 to 8 years differ markedly from the amount and varying rate of growth of the epiphysis. This marked acceleration of boys over girls can be interpreted in two ways. The diameter of the diaphysis gives significant

TABLE 13.—*Growth and Ossification of the Radius (Distal Extremity)*

$$\text{Index} = \frac{\text{Epiphysis}}{\text{Diaphysis}} \times 100$$

	City and County School						Cleveland Public School			Horace Mann School		
	Right Hand			Left Hand			Left Hand			Right Hand		
Age	Mean	Standard Deviation	f	Mean	Standard Deviation	f	Mean	Standard Deviation	f	Mean	Standard Deviation	f
					Boys							
1 year	17.4	15.53	10	....	.....	..	....	....	..	....	....	..
2 years	41.3	23.29	11	40.6	20.11	10	....	....	..	....	....	..
3 years	59.2	16.60	16	61.0	12.37	16	....	....	..	....	....	..
4 years	66.2	16.02	21	69.0	14.14	20	....	....	..	....	....	..
5 years	76.7	12.61	22	76.1	11.22	22	79.3	7.72	9	81.6	8.68	16
6 years	83.0	11.15	20	81.5	10.45	20	83.8	6.78	40	82.4	6.78	8
7 years	91.6	6.00	11	90.5	8.25	11	89.3	6.49	40	....	....	..
8 years	95.0	3.86	9	96.4	5.50	9	94.0	4.24	44	....	....	..
					Girls							
1 year	24.9	22.1	7	....	.....	..	....	....	..	....	....	..
2 years	55.7	10.90	11	55.4	10.53	10	....	....	..	....	....	..
3 years	70.3	11.31	14	69.5	10.89	13	....	....	..	....	....	..
4 years	79.4	8.66	24	79.1	8.66	24	....	....	..	....	....	..
5 years	87.5	9.05	24	85.7	8.42	24	89.1	7.01	9	88.7	6.06	11
6 years	91.0	7.23	21	90.4	6.81	21	89.3	6.72	31	96.1	3.14	9
7 years	95.5	7.80	15	94.9	7.16	15	92.9	7.31	32	....	....	..
8 years	102.8	....	5	102.6	....	5	99.3	4.81	30	....	....	..

positive correlations with stature (tables 19 and 20) which in the City and Country School is slightly greater for boys than for girls. But of much greater importance is the principle pointed out by Professor Boas [29] that in areas such as cranial diameters and the present example of the breadth of long bones, where small annual increments of growth occur in all but the first few months of life, sex differences characteristic of the adult are present throughout the growth of young children. Opposed to these are characters of comparatively rapid annual increase such as are seen in the spread of ossification where the acceleration of even the youngest girls is an expression of more advanced physiologic development.

29. Boas, Franz: Remarks on the Anthropological Study of Children, Tr. Fifteenth International Congress on Hygiene and Demography, Washington, Sept. 23-28, 1912, p. 3.

Comparison between children from the City and Country School and those from the Cleveland public school (left hands again have a small excess in diaphysis) shows the Cleveland boys of 7 and 8 smaller by one year's average, and all four groups of Cleveland girls equal to averages of City and Country School children two years younger. This is plainly explicable from stature (table 1) which, as has just been said, has a high correlation with the diameter of the shaft. A similar contrast is provided by the Sicilian infants and the younger group of boys from the Nursery School. The average diameters are: Sicilian boys, 14.7 ± 1.01, girls 13.3 ± 1.16; boys from the Nursery School 15.3 ± 0.69; statures of above 68.3, 64.3, 74.1.

Radius—Index.—The relationship of the two foregoing factors of growth and ossification as expressed by the index: epiphysis $\times$ 100 divided by diaphysis gives again clear proof of sex and age differences and displays striking uniformity in the three school groups (table 13).

For every age group from 1 to 8 years, including Cleveland girls with small epiphyses and the few children from the Horace Mann School, the mean index for girls exceeds that for boys, and with the exception of the Cleveland girls, the male standard deviations are far greater than those of the female. While the 5-year old groups from Horace Mann School corroborate the variabilities of the still younger series of children from the City and Country School, there is also reason to feel that among the boys 2 years of age, although all are in normal physical condition, there are a few with a slow rate of ossification.

Metacarpals and Phalanges.—Mention has already been made of the probable high significance in the ossification of the child played by the nineteen epiphyses for the long bones of the hand. The extreme acceleration of their appearance in girls over boys, their marked retardation in cases of malnutrition, their union with the shafts in an order opposite to that of appearance, all indicate problems of origin and function which there is neither the material nor the knowledge to solve in the present article. Unfortunately, the time of first appearance falls within the age groups of least frequency and without comparative data, but from these, some interesting relationships have been traced which will be brought forward in the concluding section.

The average number of epiphyses for metacarpals and phalanges present in the children of the City and Country School is given in table 14.

After the age of 2 years, 5 months, every girl has the full set of nineteen epiphyses.

If, as the radial index suggested, some of the younger boys are somewhat retarded, the disparity between sex rates expressed here might be modified by additions to the group or comparisons with one of

different composition, but it could hardly be erased or reduced to the same proportions in terms of years as the ossification of the radius.

Since studies of the epiphyses of normal children are scanty, a description of the order of appearance of these epiphyses is included here, which may be of some use in studies of their union.

In general, the order runs: (1) terminal phalanx of the thumb; (2) first phalanges (proximal row) in order, second, third, fourth and fifth; (3) metacarpals, second, third, fourth and fifth; the metacarpals sometimes precede the first phalanges, or they appear in pairs; (4) second row phalanges; (5) third (terminal) phalanges; (6) metacarpal —proximal—for thumb; (7) first phalanx of thumb.

In three cases, other epiphyses preceded the distal phalanx of the thumb. Centers present were as follows: metacarpals, second, third and fourth (girl, 10 months); proximal phalanges, second, third and fourth (girl, at 11 and 14 months; at 17 months thumb phalanx appeared);

TABLE 14.—*Average Number of Epiphyses for Metacarpals and Phalanges*

	Boys			Girls		
Age	Frequency	Mean	Standard Deviation	Frequency	Mean	Standard Deviation
1 year	10	2.8	3.68	7	4.7	3.77
2 years	11	8.4	4.68	11	17.0	2.34
3 years	16	14.7	3.72			
4 years	21	17.3	2.39			
5 years	22	18.9	0.62			

metacarpals and proximal phalanges, second, third, fourth and fifth (boy, at 2 years 3 months and 2 years 9 months, thumb phalanx at 3 years 3 months). This phalanx epiphysis was alone present in two cases, a boy and a girl of 9 and 11 months.

Epiphyses for the first row of phalanges preceded those for the metacarpals in ten of nineteen children, followed the metacarpals in three, and were paired with them in six instances.

For the middle row of phalanges, in four cases, when only two centers were present, the order was third and fourth finger in three cases, second and third in one case. When three centers were present (thirteen cases), the epiphysis for the fifth finger was always the one absent. The usual order for the ossification of distal epiphyses is middle finger, fourth (ten cases, middle—second, one case). In eight cases noted, the last center absent was that for the second finger five times and for the fifth finger three times. Either of these may be the last epiphysis to appear. Occasionally it is that of the metacarpal of the thumb, and often the proximal phalanx of the thumb. For these statements, records of first appearance or absence are supplemented by observations of the markedly smaller size of one of these four centers.

Of far greater interest is the incidence of proximal epiphyses for metacarpals 2 to 5. According to Rochlin,[30] proximal epiphyses for these bones appear normally only in sea mammals—sea cows, whales and seals. He does not consider it a true epiphysis in man. Among the roentgenograms of 154 children from 2 months to 10 years of age (Staatsinstitute für Röngenologie und Radiologie, Leningrad.) he found eight cases, 5.2 per cent. Scammon,[26] in his "Outline of Anatomy" gives 3 per cent. The figures from this series are much higher. Of fifty-eight boys (two more than in the rest of the study) and fifty-two girls, this anomaly of the second metacarpal occurred sixteen times; in 24 per cent of the boys (fourteen) and in 4 per cent of the girls (two). The forty-four roentgenograms from the Horace Mann School gave only one example, a boy who also had a similar condition of the fourth metacarpal. Another boy, from the City and Country School, showed a separate proximal center for the metacarpal of the fifth finger. There are no notes for the Cleveland material. Attempts to link this irregularity with retardation in the other epiphyses of the hand and of the fingers, and with the radial index, showed all but two boys and both of the girls at or above average development. Grouping by families proved more interesting. Only five of the sixteen children with this extra epiphysis had no brothers and sisters in the school. Eleven of nineteen children in seven families had unmistakable epiphyses, two cases were doubtful because of fusion, and six were absent. Four of the six were girls. A more detailed study of these cases over a five year period will be made at a later date.

Ulna—Distal Epiphysis.—The last epiphysis of the hand to be commented on is that for the distal end of the ulna. In tables 7 and 8, the time of appearance is recorded for the children of the City and Country School. The yearly percentages show the girls always a year in advance of the boys, but the record of actual first appearances gives them an average margin of only seven months. Although it is likely that in children entering the school at this age (from 5 to 6 years), the first appearance is seen only in the girls with a slower rate, still it seems that there is less sex difference in the presence of the ulnar epiphysis than in any of the carpal bones. Percentages for the children from the Horace Mann and Cleveland schools are given in table 15. The figures for Cleveland closely approximate those for the City and Country School.

A study has not been attempted of the development of this epiphysis in relation to its diaphysis and to the progress of ossification in the

30. Rochlin, D. G.: Ueber die Pseudoepiphysen und deren Bedeutung in der Endokrinologie, Ztschr. f. Anat. u. Entwcklungsgesch. **82**:358, 1927.

radius, because of its late appearance in the series, and it does not, therefore, enter into any of the formal intercorrelations. However, children with this center, from 4 through 7 years, both boys and girls in all three school groups, exhibit a marked tendency to ossification, as expressed by the radial index and the number of carpal bones, more

TABLE 15.—*Ulna (Distal Epiphysis)*

	Percentage Present at Each Age							
	5 Year		6 Year		7 Year		8 Year	
	♂	♀	♂	♀	♂	♀	♂	♀
Horace Mann school	0	27	13	100	..	..	..	..
Cleveland public school	11	44	20	52	58	81	73	100

TABLE 16.—*Ulna. Presence of Distal Epiphysis in Relation to Radial Index and Number of Carpal Bones*

Boys		City and Country School	Girls		
5 Years	3 Cases		4 Years	3 Cases	
Present index	92	Carpals	6.0	Present index	81	Carpals	6.7
Mean index	76	Mean carpals	4.2	Mean index	79	Mean carpals	5.4
6 Years	7 Cases		5 Years	8 Cases	
Present index	91	Carpals	5.4	Present index	94	Carpals	6.6
Mean index	83	Mean carpals	4.8	Mean index	86	Mean carpals	6.3
7 Years	6 Cases		6 Years	12 Cases	
Present index	94	Carpals	7.0	Present index	94	Carpals	7.0
Mean index	92	Mean carpals	6.4	Mean index	91	Mean carpals	6.9
			7 Years	1 Without Ulna	
			Present index	76	Carpals	7.0
			Mean index	96	Mean carpals	7.1
		Horace Mann School			
6 Years	1 Case		5 Years	3 Cases	
Present index	95	Carpals	7.0	Present index	93	Carpals	6.7
Mean index	82	Mean carpals	5.0	Mean index	89	Mean carpals	6.5
		Cleveland Public School			
6 Years	8 Cases		6 Years	16 Cases	
Present index	91	Carpals	5.6	Present index	93	Carpals	6.8
Mean index	84	Mean carpals	5.2	Mean index	89	Mean carpals	6.6
7 Years	23 Cases		7 Years	26 Cases	
Present index	91	Carpals	6.8	Present index	96	Carpals	7.0
Mean index	89	Mean carpals	6.3	Mean index	93	Mean carpals	6.9

advanced than their group means in either trait, and in the 7 year group, the only girl still lacking the ulnar epiphysis has an index twenty points below the average. These relationships will be found in table 16.

ERUPTION OF THE TEETH

The records of eruption of the first and second dentition have not afforded uniform and significant material for relation to stature, weight and ossification of the hand. In groups 3, 4 and 5, practically no new

teeth appear. Groups 1 and 2 are too small to afford reliable data for correlations; the same is true for groups 7 and 8. For the boys and girls 6 years of age, six of the forty-one cases had no dental record within several months of the roentgen-ray date. Averages calculated for the remainder showed too high individual variation to allow agreement with Bean [31] and Cattell [32] that "dentition is the best available method for determining the physical development of children," and is "more convenient and more exact as a means of determining the physiological standard than stature, weight, or growth of bones."

Surveying briefly the data on deciduous teeth, from the groups represented in the study, there is first of all the average number of incisors present for the Sicilian infants and the eight youngest boys from the Nursery School. The regular 1 year groups have too long an age range to be of any value. The number of teeth in these three series follows stature, weight and also age, each division being one month younger than the preceding. Hence there is: boys from the Nursery School incisors 4.6 ± 3.79; Sicilian boys 2.6 ± 2.63; Sicilian girls 1.4 ± 2.12. The enormous standard deviations resulting from the number of cases in which no teeth were present, illustrate the skewness of the trait for these groups.

Eleven boys and ten girls from 18 to 29 months (2 year group) show an almost identical development. The boys average seventeen teeth, the girls, with a mean age of 2 months less than the boys, sixteen teeth. Professor Boas [33] found the same lack of sex difference until the eruption of the second deciduous molar. No correlation with stature or ossification for the 2 year old children was attempted, because of the low frequencies.

In the groups of children 3 years of age, one boy (2 years, 10 months) still lacked the upper second molars, and another boy at 3 years, 1 month, known to have an early rachitic history and slow ossification, had only sixteen teeth. The upper right second molar of a girl of 2 years, 10 months was absent and both upper molars of another of 3 years, 3 months had just broken through the gums. Excepting the appearance of the left central incisor in the mandible of a boy at 5 years, 2 months, there are no other appearances of teeth until the 6 year groups.

The means and standard deviations for the number of permanent teeth erupted in boys and girls of 6 are as meaningless as those for the

31. Bean, R. B.: The Eruption of the Teeth as a Physiological Standard for Testing Development, Pedagogical Seminary **21**:612 (Dec.) 1914.

32. Cattell, Psyche: A Scale for Measuring Age, School and Society, vol. 27, p. 52.

33. Boas, Franz: The Eruption of Deciduous Teeth Among Hebrew Infants, J. Dent. Research **7**:253, 1927.

infants. These averages (boys, 1.7 ± 2.44; girls, 1.5 ± 2.03) are again explained by the fact that 61 per cent of the boys and 53 per cent of the girls still have only deciduous dentition. The development of the boys ranges from two lower incisors to two lower incisors and four molars; two of the girls have only one incisor erupted. Although children from the City and Country School are always less developed than Bean's standard of two lower incisors and the four first molars for 50 per cent of American boys and girls between 5 and 6 years or Boas'[34] percentages for upper teeth (6 years; central incisors, boys, 30 per cent, girls, 38 per cent; first molars, boys, 65 per cent, girls, 83 per cent), the averages for number of permanent teeth recorded at the annual medical examinations in the school from 1919 to 1926 are higher

TABLE 17.—*Permanent Teeth of Tall and Short Children from City and Country School*

Age	Mean Difference* Between Tall Children and Entire Group	Mean Number of Permanent Teeth for Tall Children	Mean Number of Permanent Teeth for Entire Group	Mean Difference* Between Short Children and Entire Group	Mean Number of Permanent Teeth for Short Children	Mean Number of Permanent Teeth for Entire Group
			Boys			
5 yr., 6 mo.	1.8	0.3	0.2	2.1	0.1	0.2
6 yr.	1.4	3.2	2.1	2.1	0.9	2.1
6 yr., 6 mo.	2.1	3.6	3.2	2.5	2.4	3.2
7 yr.	1.8	6.7	6.2	2.2	4.8	6.2
7 yr., 6 mo.	1.7	7.4	7.1	2.1	7.0	7.1
			Girls			
5 yr., 6 mo.	1.6	0.3	0.1	1.9	0.0	0.1
6 yr.	2.2	2.1	2.3	1.8	1.7	2.3
6 yr., 6 mo.	1.5	4.7	4.7	1.5	3.3	4.7
7 yr.	2.2	7.5	7.6	2.1	6.5	7.6
7 yr., 6 mo.	2.7	9.7	8.9	1.9	8.9	8.9

* Difference measured in inches.

than for the smaller groups included in the present study. Relating the number of teeth to the stature by the calculation of separate dental averages for boys and girls, more than one half inch above and below their age means for height standing measured at the same examinations, it was found that the short children consistently have fewer teeth than the average for their age. The tall children, however, seldom exceed the mean (table 17).

INTERRELATIONSHIPS OF OSSIFICATION AND GROWTH

The quantitative description of ossification in the hands of young children from two private schools and a group from a public school indicated various interrelationships of progress in different epiphyses and centers, of extent of ossification to growth in breadth of bone, and of both these factors to stature and weight. The association of

34. Boas, Franz: Statistics of Growth, p. 34.

the distal epiphysis of the ulna with more than average development of carpal centers and a higher radial index has already been fully described (table 16). The relationships which the size of radial epiphysis, diameter of radial shaft and the radial index, number of epiphyses for metacarpals, and phalanges, and number of centers for carpal bones, bear to one another and to height and weight have been calculated for all groups in which the frequencies permitted by the adaptation of the Pearsonian coefficient of correlation.

$$\frac{[xy]}{\sigma_x \sigma_y} \text{ worked out as}$$

$$r = \frac{\sigma^2_x + \sigma^2_y - \sigma^2_{x-y}}{2\sigma_x \sigma_y}$$

TABLE 18.—*Growth and Ossification of the Radius (Distal Extremity), Correlations*

	City and Country School					Cleveland Public School			Horace Sieil-Mann Ian School	Infants
Age.....	3 Yr.	4 Yr.	5 Yr.	6 Yr.	7 Yr.	6 Yr.	7 Yr.	8 Yr.	5 Yr.	1 Yr.
Correlations										
Boys										
Epiphysis—diaphysis.....	+0.27	+0.18	+0.40	+0.21	.....	+0.57	+0.66	+0.86	.....	.....
Epiphysis—number carpals	+0.42	+0.57	+0.68	+0.59	.....	+0.31	+0.66	+0.38	+0.66	.....
Diaphysis—number carpals	+0.17	+0.17	+0.26	+0.10	.....	+0.02	+0.43	+0.36	.....	+0.44
Index*—number carpals...	+0.43	+0.54	+0.64	+0.56	.....	+0.36	+0.54	+0.17	.....	.....
Girls										
Epiphysis—diaphysis.....	+0.20	+0.27	+0.25	+0.38	+0.44	+0.56	+0.73	+0.85	.....	.....
Epiphysis—number carpals	+0.02	+0.56	+0.67	+0.55	+0.35	+0.57	+0.31	.....	.....	.....
Diaphysis—number carpals	+0.27	+0.37	+0.10	−0.26	+0.11	+0.03	−0.09	.....	.....	+0.57
Index*—number carpals...	+0.57	+0.39	+0.59	+0.72	+0.31	+0.68	+0.52	.....	.....	.....

* Index $= \frac{\text{Epiphysis}}{\text{Diaphysis}} \times 100$

While the actual size of the coefficients are unreliable because of the small number of cases, the uniformity of position held by correlations throughout the majority of the groups proves the integrity of the biologic relationships thus expressed.

The correlations of the factors of growth and ossification of the radius with each other and with the number of carpal bones (table 18) are higher between factors of ossification—epiphysis—number of carpal bones, index—number of carpals—than between diaphysis and epiphysis until the age of 7, when the diameters of the epiphysis and diaphysis are practically the same. In twelve of fourteen groups, the diaphysis with the number of carpal bones gives the lowest coefficient of the hand.

Further evidence that ossification tends to proceed as a whole is furnished by correlations for number of metacarpals and phalanges of girls 2 years of age and boys of 2, 3 and 4 years with the traits related

in table 18. The *r's* are higher with radial epiphysis than with the number of carpal bones. The number of epiphyses bears a close relationship to the size of the epiphysis for radius, much more pronounced than does the number of carpal bones. For girls 2 years of age, radial epiphysis—epiphyses of the hand + 0.55; number of carpal bones—number of epiphyses + 0.08. The same coefficients for 2 year old boys are + 0.50

TABLE 19.—*Correlation of Stature and Weight with Growth and Ossification of the Hand*

	City and Country School					Horace Mann School	Sicilian Infants
Correlations							
	Boys						
Age	3 Years	4 Years	5 Years	6 Years	7 Years	5 Years	1 Year
Stature—weight	+0.94	+0.75	+0.86	+0.75	.....	.....	+0.88
Stature—epiphysis	+0.48	+0.32	+0.45	+0.25	.....	.....	.....
Stature—diaphysis	+0.72	+0.61	+0.75	+0.53	.....	+0.74	+0.70
Stature—index*	+0.38	+0.19	+0.18	+0.11	.....	.....	.....
Stature—number carpals	+0.08	+0.18	+0.28	+0.10	.....	.....	+0.08
Weight—epiphysis	+0.56	+0.25	+0.39	+0.24	.....	.....	.....
Weight—diaphysis	+0.61	+0.58	+0.61	+0.30	.....	.....	+0.72
Weight—index*	+0.48	+0.12	+0.18	+0.13	.....	.....	.....
Weight—number carpals	−0.01	+0.13	+0.18	0.00	.....	.....	−0.01
	Girls						
Stature—weight	+0.87	+0.68	+0.75	+0.73	+0.86	.....	+0.89
Stature—epiphysis	+0.63	−0.17	+0.28	+0.18	+0.56	.....	.....
Stature—diaphysis	+0.15	+0.47	+0.34	+0.57	+0.60	.....	+0.76
Stature—index*	+0.60	−0.40	+0.03	−0.20	+0.21	.....	.....
Stature—number carpals	+0.51	+0.10	+0.01	−0.37	+0.42	.....	+0.61
Weight—epiphysis	+0.50	0.00	+0.43	+0.23	+0.39	.....	.....
Weight—diaphysis	+0.06	+0.22	+0.61	+0.72	+0.76	.....	+0.76
Weight—index*	+0.49	−0.30	+0.05	−0.27	−0.10	.....	.....
Weight—number carpals	+0.40	+0.14	+0.18	−0.36	+0.19	.....	+0.32

* Index $= \frac{\text{Epiphysis}}{\text{Diaphysis}} \times 100$

TABLE 20.—*Averages of Correlations from Table 19, City and Country School*

	City and Country School	
	Boys	Girls
Stature—weight	+0 82	+0.76
Stature—epiphysis	+0.37	+0.21
Stature—diaphysis	+0.64	+0.44
Stature—index	+0.21	+0.11
Stature—number carpals	+0.17	+0.08
Weight—epiphysis	+0.35	+0.28
Weight—diaphysis	+0.52	+0.49
Weight—index	+0.21	−0.07
Weight—number carpals	+0.08	+0.08

and + 0.05. At 3 and 4 years, *r* for radial epiphysis—epiphyses of the hands is + 0.73 and + 0.71; for carpals with epiphysis + 0.28 and + 0.29. Coefficients for epiphyses and index follow closely those for radial epiphysis, + 0.68 and + 0.69.

All of this strongly indicates the interdependence of ossification in the hand, of which the development of carpal bones is the least vital part, and the comparatively slight relationship of this process to growth of bone as represented by the diaphysis of the radius before the age of 7.

In relation to the total size of the child as expressed by stature, a different order of characters appears (tables 19 and 20).

All groups of boys have a coefficient for stature and diaphysis second only to the obviously high *r's* for stature and weight. In two of the three groups of girls where other *r's* precede stature-diaphysis, the second *r* is weight-diaphysis.

Between stature and epiphysis for the radius there is, in all but two groups of girls, significant correlation, ranking in most cases after stature-weight and the *r's* of diaphysis with stature and with weight. Coefficients for weight and ossification follow closely the coefficients for stature and the same traits, but are almost always smaller.

Epiphyses for metacarpals and phalanges for boys give the following figures with stature and weight: with stature, 3 years + 0.40, 4 years + 0.41; with weight, + 0.51 and + 0.32. The same groups show much lower coefficients with the number of carpal bones (table 19).

The slightest relationship in the entire series exists between the weight and number of carpal bones, with the stature and carpal bones only slightly higher.

It seems, then, safe to conclude that ossification is closely related throughout the hand of children from 1 to 8 years and that there exists a definite interrelationship between ossification and gross bodily size, but that this correlation is less than that between the actual growth of bone and the child's stature and weight.

JUVENILE ACRODYNIA *

C. W. WYCKOFF, M.D.
CLEVELAND

In 1914, Swift of Australia reported several cases with a symptom-complex supposedly different from any ever reported. From the unusual character of this clinical entity, he ventured to name the condition erythredema, because of one of the most cardinal symptoms, a dull bluish-red swelling of the hands and feet. Since this time, two hundred or more cases have been reported by English, Canadian and American physicians.

The disease affects infants and young children mainly between the ages of 12 months and 4 years, and is characterized by extreme fretfulness, marked neuromuscular disturbances, sleeplessness and a dull red or pink rash of varying character sometimes over the entire body, but involving mainly the hands and feet. The first American to report such cases was Bilderback [1] in 1920.

Clubb of Australia has called it the "pink disease." Paterson and Greenfield of England [2] have termed the ailment "erythroedema polyneuritis." Canadian observers, as Brown, Courtney and MacLachlan [3] and others, as well as most American authors on the subject, such as Byfield,[4] Zahorsky [5] and Weston,[6] have reported such cases under the heading of possible acrodynia. This is undoubtedly the right name, the condition being an old disease rediscovered. But there are so many salient points of difference between acrodynia in adults, first described during the early part of the nineteenth century and the cases found during the past decade that I believe the term juvenile acrodynia should be used.

ETIOLOGY

Only by the process of elimination of other factors can one say that a subacute infection is the most likely progenitor of the more or

* Received for publication, Sept. 14, 1928.

1. Bilderback, J. B.: Group of Cases of Unknown Etiology and Diagnosis, Northwest Med. J. **19:** 263, 1920.

2. Paterson, D., and Greenfield, J. G.: Erythroedema Polyneuritis (The So-Called "Pink Disease"), Quart. J. Med. **17:**6, 1923-1924.

3. Brown, A.; Courtney, A. M., and MacLachlan, I. F.: Clinical and Metabolic Study of Acrodynia, Arch. Pediat. **38:**609, 1921.

4. Byfield, A. H.: A Polyneuritic Syndrome Resembling Pellagra-Acrodynia (?) Seen in Very Young Children, Am. J. Dis. Child. **20:**347 (Nov.) 1920.

5. Zahorsky, J.: Acrodynia in Infants, J. Missouri M. A. **190:**296, 1922.

6. Weston, W.: Acrodynia, Arch. Pediat. **37:**513, 1920.

less chronic toxemia found in these cases. No writers so far, with the exception of Byfield and Rodda, have suggested an infection. The former even designates the infection as a postinfluenzal radiculitis found at autopsy in one of his cases. Then, also, the history in several of his cases showed evidence of influenza.

Nearly all the writers on the subject mention infection of the upper respiratory tract as a precursor and as an accompaniment of this symptom-complex, but none of the others favor the influenzal theory. In my experience with twelve cases during the past ten years, the preceding ailments were pertussis, gastro-enteritis, pyelitis and simple colds in the head and in three cases there was no apparent disease beforehand.

As to the question of a disease due to a deficiency in food, this may be ruled out from the facts that in the majority of cases the diets had been perfect. In some cases the patients had been perfect breast-fed babies, others had been bottle fed, and still others had been on a mixed diet with an ample supply of all the necessary food elements. In 1922, Field [7] made many protein tests in a case in which negative reactions were obtained.

The disease is independent of the season of the year, as cases have been reported as occurring throughout the entire year. As to countries in which the disease is observed, cases have been reported from only Australia, England, Canada and the United States. Both sexes are similarly affected. Living conditions do not have any bearing on the condition; in fact, in most cases the diet and surroundings have been perfect, and the disease has occurred in both rural and urban sections. The results of all laboratory examinations are negative, as are the Wassermann and the Pirquet tests; the urine and stool are normal and the blood culture is negative. Field alone has determined the blood chemistry in a case, but with negative results. Brown, Courtney and MacLachlan found a lowered nitrogen balance in one case, studied from a metabolic standpoint, and a negative balance of bases in another. Observers have not found anything abnormal in the microscopic examination of the blood, except a leukocytosis ranging from 10,000 to 40,000, a fact which certainly indicates an infectious process.

SYMPTOMATOLOGY

The literature on this subject is most striking in that the description of symptoms given by various authors is exactly the same. The symptom-complex is so unusual, yet so evident, that once seen and recognized it will never be forgotten. In view of the fact that 99 per cent of the patients are less than 6 years of age, the symptoms are

7. Field, M. C.: Case of Erythroedema, Arch. Pediat. **39**:116, 1922.

entirely objective. The parents complain of extreme restlessness, sleeplessness and irritability of a child who heretofore had shown the opposite tendency. It never smiles and it refuses to play or to be entertained. While lying down, its head is buried in a pillow, face down; when sitting, the body is in a crouching position, the head and trunk bent forward, so that the abdomen may rest on the thighs. The picture is that of most abject wretchedness.

The cardinal symptom is the peculiar redness and swelling of the hands and feet, with a moderate degree of desquamation and a cold, clammy feeling. There may be a constant rubbing or wringing of the hands and feet, or the child may chew its fingers and toes. A rash appears from three weeks to four months after the onset, according to the cases reported by different observers, but in most cases it appears fairly early and involves almost the entire body; however, there is nothing characteristic about this symptom.

One may easily be misled and may diagnose the condition as one of the acute exanthemas, as it may resemble scarlet fever, measles, German measles, acute eczema or infantile erythema. Many cases show a more or less diffuse erythema with minute papules over the most inflamed parts. Sometimes the rash looks like a severe prickly heat rash; then again irregularly inflamed patches appear over the trunk. The eruption is not constant; it appears and disappears throughout the course of the disease. Profuse sweating is almost always present, giving the skin a cold, clammy feeling. The hair comes out easily, either falling out or being pulled out by the child in its nervous, negative mental attitude. Likewise, the finger-nails or toe-nails may fall off, leaving no sign of an inflammatory condition. The teeth also become loosened and may fall out from constant grating, the gums showing no visible pathologic condition.

Anorexia is another constant symptom and the most serious of all. It is so marked in many instances that unless gavage is resorted to, the child dies of starvation. The intestinal tract does not show any symptoms of consequence, nor is the urinary function disturbed, except that the quantity is diminished because of insufficient fluid intake. There is a varying degree of photophobia in all cases. The temperature may be normal, but there is more apt to be an elevation to 100 degrees throughout the illness, and this to an unsuspecting examiner may suggest a tuberculous lesion somewhere in the body.

Asthenia is also a constant symptom, and while the greatly diminished intake of food may account in part for this, the great degree of muscular hypotonicity would account better for the extreme asthenia in some cases.

Typical beefy red hands in juvenile acrodynia. (The subject of this illustration was a case of one of my associates, Dr. Paul G. Albrecht.)

PHYSICAL CHANGES

Several of the physical changes have already been mentioned. The mucosa of the nose, mouth and throat shows considerable irritation at times, and there is a thin mucous discharge. The tongue is moderately coated; the abdomen, lungs and heart are normal. The condition of the skin, hands and feet has previously been described. The degree of emaciation depends on how long the child has been ill, and on how successful the parent has been in forcing nourishment. Nearly all patients, however, have a small amount of subcutaneous fat. The muscles are soft and flabby and show a marked degree of hypotonicity; this may be so extensive that the child will not be able to hold up its head, as noted by Paterson and Greenfield. Actual motor paralysis does not occur, according to all the articles consulted and in my experience, for the child can use all muscles, but the weakness seems to be due entirely to tonelessness of the general musculature.

The nervous system, however, shows most marked changes. From the irritability and general wretched picture the child presents one judges that he suffers from a dull, nagging pain of some description, and this is most likely a peripheral neuritis, as suggested by Byfield, Paterson and Greenfield. Sensation to pain from pin pricks is greatly diminished over the entire body, and in certain areas is lost entirely. The tendon muscle reflexes are markedly diminished or absent. Ulceration of the tongue, cheek, palms and soles and loss of teeth, nails and hair, without an attendant inflammatory process, have been reported, which, of course, indicate trophic involvement of the nerve.

Pathology.—Because of the meager number of cases in which the disease ended fatally, and the newness of this disease, only three cases so far have come to autopsy, but these have shed considerable light on this peculiar disease. Byfield reported the first case, and from his observations suggested the presence of a postinfluenzal radiculitis or sensory polyneuritis. Swift, however, claims that the majority of cases occurred in children not previously affected by influenza.

In Byfield's case, a generalized tuberculous infection caused the fatal termination. On examining the spinal cord, he found occasional involvement of an anterior horncell, gliosis of the central canal of the entire cord and edema of the sensory roots. Byfield claimed that the falling out of the hair and the loss of teeth, without pathologic change, point clearly to involvement of the fifth cranial nerve.

The autopsy in the other two cases was performed by Paterson and Greenfield; in one case, the patient died from intestinal intussusception, in the other, from a generalized tuberculosis. In the latter, the changes in the nervous system were naturally seen at their worst, and these authors claimed that the case proved conclusively that the disease is a polyneuritis

affecting particularly the peripheral parts of the nerve trunks. Their histologic examination showed considerable myelin degeneration and destruction in some of the peripheral nerve fibers, increasing in degree and extent on passing to the peripheral parts of the nerves. They did not find clear evidence of bacterial invasion of either the central or the peripheral nervous system, although from the histologic appearance they believed the polyneuritis due to the toxin of some micro-organism rather than to a disorder of metabolism such as is found in beriberi and pellagra.

They confirm Byfield's claim that the condition is a peripheral neuritis involving mainly the sensory nerves and showing marked vasomotor disturbances of the extremities. The pathologic changes and the conclusions of these three investigators are convincing to any one who has studied these cases clinically.

Differential Diagnosis.—The first disease that one should have in mind is the form of acrodynia or "painful extremities" or epidemic erythema occurring in adults. This was first described by Frenchmen in 1828 following an extensive epidemic of influenza in Paris and its environs. About 40,000 cases were reported. It occurs in old or improperly nourished adults. Its symptoms are those of polyneuritis. It begins with severe intestinal cramps, and the general nutrition is greatly lowered. There are burning pains in the palms and soles with marked hyperesthesia, which becomes most distressing. The pain is accompanied by a severe erythematous rash most marked on the extremities, and in some cases developing into an intense pigmentation. The disease is afebrile. There is photophobia and increased lacrimation. The condition lasts about four weeks. In the juvenile type, it lasts from two to eighteen months; it is not epidemic, and the cases are rare. There is a low fever, and no gastro-enteral disturbance; only young children are affected. The skin manifestations, the eye signs and the polyneuritic signs are practically the same. Nothing is known as to the etiology or pathology of acrodynia, and unfortunately but little is known of the juvenile type.

Beriberi and pellagra must also be considered; however, these diseases are distinctly metabolic disturbances due to definite deficiency in diet. Arsenical poisoning should also be mentioned, but the rash, the condition of the hands and feet, and the history, will easily guide one in ruling this out. Erythromelalgia should also be mentioned, but here again the distinction is obvious, as here there is only the symptom of pain, and it is confined to adults.

Treatment.—In a recent treatise by Rodda, he claims fairly prompt cessation of symptoms by excising the tonsils and adenoids, if the cases are not far advanced. This would seem rational when there is any

marked degree of infection of the upper respiratory tract and the physical condition will permit. For the nervous symptoms, sedatives or hyponotics are useless. For the skin eruption and itching, calamine lotion profusely applied gives considerable relief. The principle object should be to maintain a fair state of nutrition; a rational diet suitable for the particular age of the patient is suggested, which the child shoul l be urged and forced to follow. I have resorted to mixtures of buttermilk, as this is apparently better tolerated than milk in any other form. If the anorexia is complete, gavage should be resorted to and continued sometimes for many weeks, or the child will sink to such a low stage of starvation that any mild added infection may cause death.

REPORT OF CASES

CASE 1.—B. P., a girl, aged 3 years, was first seen in May, 1913. The complaint was constant restlessness, irritability day and night and loss of appetite for six weeks. The attack was preceded and accompanied by marked pyelitis. The child rubbed and chewed the hands and feet constantly. A fine rash was present—at times over the entire body. It was difficult to feed the patient, although there was no digestive upset, cold in the head, throat trouble or pulmonary symptoms. The child moved about constantly in bed biting her fingers and rubbing her feet together; she seemed to be in a constant state of partially suppressed pain. The skin was clammy and the hands and feet were bluish red, swollen, cold and desquamating. A miliary-like eruption was present over the entire body. The subcutaneous tissues were soft; the muscles were rather toneless. The reflexes were sluggish. The patient had a moderate degree of photophobia; otherwise the results of the physical examination were negative. The temperature was 100 F.; pulse rate, 140, and respirations, 30; the leukocyte count was 14,000. The Pirquet test was negative; the urine showed an abundance of pus cells. The symptoms lasted about four months and were followed by complete recovery.

CASE 2.—G. O., a boy, aged 18 months, was first seen in May, 1914. The complaint was absolute refusal of nourishment. Four weeks previous to the time of observation the child had a moderately sore throat and loss of appetite and was restless and irritable. Aften ten days a fine raised rash appeared over the trunk; the family physician thought it was scarlet fever. The rash, however, had persisted; sometimes it disappeared, and then it returned in patches. The child seemed to have pain all over the body at times and would double up. He had moderate photophobia; the skin was clammy and inelastic, and there was marked loss of subcutaneous tissues. A few patches of red papules were scattered over the trunk; the hands and feet were moderately swollen, dull red, cold and desquamating. The muscles were flabby, the child seemed extremely weak; yet he had a strong cry, the tongue was coated, the throat was moderately inflamed and the tonsils were not especially affected. Rhinitis was present. There was no apparent digestive abnormality; the lungs and heart were normal; the reflexes were absent; the temperature was 101 F.; the pulse rate, 130; the leukocyte count was 15,000; the urine was normal. The child was gavaged for two months. Recovery was complete after a period of three months.

CASE 3.—D. H., a boy, aged 3 years, was first seen in June, 1920. The complaint was restlessness, loss of appetite and fever for two months. The illness started following an attack of influenza, during which the child had sore throat, running

nose and loose cough. The bowels were also upset, and the patient had one or two loose greenish movements a day. Eruptions were also present which at times looked like measles, then again like a sweat rash. The patient bit his hands a great deal and grated his teeth until the mother feared they would fall out. He assumed a crouching position most of the time. The temperature ranged from 100 to 101 F. The patient was extremely emaciated, restless and irritable; he seemed to have a constant pain somewhere in the body. He would wring his hands and rub his feet together a great deal, and seemed to have considerable photophobia. The skin was cold and damp and extremely inelastic. He had occasional dull red papules over the trunk. The hands and feet were somewhat swollen and were dull, bluish red and desquamating. The musculature was toneless; the gums were swollen and red, the tongue was coated and the throat was moderately injected. A thin, watery nasal discharge was present; the lungs and heart were normal; the abdomen was scaphoid with negative observations. The reflexes were absent; the temperature was 100 F.; the pulse rate, 140, and respirations, 30; the white blood cell count was 16,000. The Pirquet test was negative. The urine was normal. The child was fed on buttermilk and made an uneventful recovery after an ilness of eight months' duration.

Case 4.—M. F., a girl, aged 2½ years, was first seen in June, 1921. The light hurt the child's eyes; she was extremely irritable and refused nearly all food. The child had always been well up to one month previous to the present illness, when she began to feel bad. She had a constant slight watery nasal discharge. There was no fever, cough, or vomiting and no disturbance of the bowels; nothing would please the child. The nights were bad. She refused all food with the exception of a little milk. Well marked photophobia was present with slight redness of the conjunctiva and slightly increased lacrimation. The child was extremely restless, and did not seem to be comfortable in any position. She showed considerable loss in weight. The skin was cool and slightly damp from perspiration; it was pale and no rash was present, but a fine rash resembling that in scarlet fever appeared later. Only the postcervical glands were enlarged. There was marked muscular hypotonicity. The mucous membranes of the mouth and throat were moderately injected. The tonsils were somewhat enlarged and spongy; adenoid tissue was abundant. The lungs and heart were normal except for an increased rate of 130 per minute. The abdomen was normal. The reflexes were sluggish. The attack lasted three months after which there was complete recovery.

Case 5.—L. M., a boy, aged 2½ years, was first seen in February, 1922. The child whined continuously day and night and refused food. He had pertussis for ten weeks just preceding these peculiar actions. Ten days prior to his visit, there was a fine, dull red, papular rash over the entire body; this disappeared at times. The bowel movements were loose and again the patient was constipated. There was a low fever most of the time. The child was terribly irritable and flighty and chewed his hands and wrists a great deal; he grated his teeth continuously. Light was painful to the eyes. There was a constant discharge from the nose. The child sweat a great deal. He doubled up most of the time. There was moderate redness of the conjunctiva, but no lacrimation; the skin was cold and damp; a fine, dull red, papular eruption was present over the body. There were no glandular enlargements. The hands and feet were swollen, dull red, desquamating and extremely clammy. The mucous membranes of the mouth, throat and nose were considerably injected. The tonsils and adenoids were not hypertrophied. The first molars and canine teeth fell out from constant grating. The lungs and heart were normal, except for the increase in rate of the latter to 140 per minute. The abdomen was normal. There

was a tremendous loss in weight later on, so that the child had to be gavaged for six weeks. There was marked hypotonicity of the muscles. The reflexes were absent; sensations to pain and temperature were accentuated. The Pirquet reaction was negative; the leukocyte count was 15,000. The urine was normal. Complete recovery followed an illness of eight months.

Case 6.—E. S., a girl, aged 11 months, was first seen in June, 1922. She slept fitfully day and night, cried most of the time and took only a little nourishment. She was bottle fed and had always been well. She was happy and had regular habits until a month before the present illness. She rubbed her hands and feet a great deal. The stomach was never upset; bowel movements were normal until during the past illness when the child became constipated; at times, however, the movements were loose. The child was extremely restless and fussy. She wanted to bury her face in a pillow all the time and assumed a crouching position as if in abdominal pain. A coarse blotchy skin eruption was present over the trunk. The hands and feet were moderately swollen and dull red, desquamating, cold and sweaty. There were no glandular enlargements. The mucous membranes showed inflammation in the mouth and throat. The tonsils were not hypertrophied. The adenoids were not present; the lungs and heart were normal except for an increased rate to 140 per minute. The abdomen was normal. The reflexes were sluggish; the skin sensations to pain and temperature were apparently accentuated. Fever was not present. After three months, recovery was complete.

Case 7.—M. H., a girl, aged 3 years, was first seen in September, 1922. She sat doubled over all of the time and cried if spoken to; she wished to be let alone. She bit her fingers constantly. Three weeks before the present illness she ate a large quantity of canned cherries and had a severe attack of diarrhea. Since that time a blotchy eruption appeared at times all over the body. The skin was cold and clammy. She slept fitfully, and refused nearly all food. The bowels moved only after an enema. The child was extremely irritable. She sat with her head bent forward with the trunk resting on the thighs. Photophobia was marked. The skin was cold and damp; rash was not present, and there were no glandular enlargements. The mucous membranes of the mouth, throat and nose were normal. The hands and feet were moderately swollen, cold and dull red. Areas of well marked hyperesthesia were present over the trunk. The lungs and heart were normal. The abdomen was normal. The reflexes were absent; there was marked loss in weight. Great muscular weakness was evident. Fever was not present. The leukocyte count was 18,000. The urine was normal. The illness lasted for a period of two and a half months, after which there was complete recovery.

Case 8.—B. C., a boy, aged 15 months, was first seen in May, 1923. He refused all nourishment and was restless and irritable day and night for one month. He had always been well until one month previous to the present illness, when he had a slight cold in the head. He lost his appetite and refused to sleep more than one or two hours at a time during the night or day. There was no stomach or bowel disturbance. He refused to be entertained, cried if talked to and wanted to bury his face in a pillow and rest in a crouching position all the time. He did not have a fever. There was a marked loss of subcutaneous tissues; the muscles were soft and showed marked weakness. The child showed some photophobia and was restless. The skin was cold and clammy and showed a fine, dull red, papular eruption over the trunk. There were no glandular enlargements. The mucous membranes of the mouth, throat and nose were inflamed. The tonsils were moderately hypertrophied and spongy. The adenoids were moderately enlarged. The lungs and heart were normal except for an increase in the rate of the latter to 140 per minute.

The abdomen was normal. The reflexes were absent. The skin sensations to pain and temperature were more acute than normal. Gavage was resorted to for seven weeks. After five months complete recovery resulted.

Case 9.—E. K., a boy, aged 16 months, was first seen in March, 1924. He scratched continuously and was irritable for one month. He had always been well previous to an attack of whooping cough during January and February, 1924. At the end of the siege he seemed to become more and more irritable and restless at night, although the cough was much better. He had a constant cold in the head. The hands and feet became red, cold and dry. When sitting, he always leaned forward with the abdomen resting on the thighs. The child looked the picture of abject misery. His eyes were half closed and he assumed a half crouching position when sitting as if in constant abdominal discomfort. He was much emaciated; the muscles were soft and flabby. The skin was cold and moist and was covered with a fine, dull red, papular rash, showing evidences of great amount of scratching. The hands and feet were dull red, swollen, desquamating and moist. The eyes were sensitive to light. The conjunctiva showed catarrhal inflammation. The ears were normal; the tongue was clean; the tonsils were neither enlarged nor inflamed. There was a moderate amount of adenoid tissue. The nasal mucosa was inflamed and moist. There was no enlargement of the lymph glands. The lungs and heart were normal; the pulse rate was 130 per minute. The abdomen was normal and rather scaphoid. The reflexes were not present. The skin sensations to heat, cold, pain and touch were greatly exaggerated in some areas. The urine was normal. The leukocytes numbered 18,000. The Pirquet reaction was negative. While the appetite was slight, enough food could be forced on the child to sustain him. After a period of four months, there was complete recovery.

Case 10.—R. S., a girl, aged 19 months, was first seen in May, 1924. She cried constantly and sat in a doubled up position. The child had never been ill, outside of frequent colds, until May 1 when she took a slight cold, grew irritable, refused most of her food, fretted all night and would sit bent over most of the time, chewing her fingers and toes and then rubbing her hands and feet. After three weeks a fine rash appeared over the body. The child seemed to be in great distress. She did not want to be touched or looked at. She was much underweight. The skin was inelastic, and a fine, papular eruption which looked like a miliary eczema was present over the trunk. There was rather marked loss of muscle tone all over the body; the hands and feet were moderately swollen, cold and clammy and were bluish red. The eyes showed moderate photophobia. The ears were normal. The nasal mucosa was red and was covered with much mucus. The gums were red and spongy; the tonsils were not hypertrophied and appeared to be normal. The adenoids were moderately enlarged. There was no enlargement of the lymph glands. The lungs and heart were normal. The reflexes were sluggish. There was no apparent change in the skin sensations. The urine was normal. The leukocytes numbered 22,000. The Pirquet test was negative. The child took a moderate amount of milk all through the period of sickness. Complete recovery followed after a period of two and a half months.

Case 11.—In Peter W., my youngest son, aged 2 years, the condition was first observed in September, 1924. There was loss of appetite, and a complete change from a sunny to a morose disposition. For two weeks prior to the present symptoms there was slight enteritis and loss of appetite and energy. He refused to play, but slept well at night. He did not cry but wished to be let alone. He perspired a great deal. After three weeks a red blotchy eruption appeared scattered over the trunk; this appeared like the rash caused by the ingestion of certain food. The

hands and feet began to swell and were cold, dull red, moist and later desquamated. He did not seem to have any pain. The patient was well nourished; he was not especially uncomfortable but preferred to be let alone. The muscular tone was somewhat less than normal. The skin was cool and clammy. The eyes, ears, mouth, nose and throat were normal. The lungs and heart were normal; the abdomen was normal. The reflexes were absent. The skin sensations were normal. The urine was normal. The white blood cells numbered 14,000. Recovery was complete after eight weeks.

CASE 12.—N. B., a boy, aged 18 months, was seen in October, 1925. He was irritable night and day and had a poor appetite for four weeks. He had whooping cough prior to the onset of the present symptoms and slept poorly at night. He seemed to be weak, not wishing to hold his head up at times. He took little food and drank only a small amount of milk. The stomach was not upset, and the bowel movements were normal. He seemed to dislike a moderately bright light. He had considerable rash over the body at times, occasionally fine, then coarse and blotchy. He refused to play and was moderately fussy when disturbed. He hung his head on his chest, had his fingers in his mouth all the time and chewed and bit his hands. His feet were swollen, bluish red, cold and clammy. The skin was otherwise normal. The eyes showed moderately inflamed conjunctivae. The ears, nose and teeth were normal; the tongue was clean; the throat was normal. There was no enlargement of the lymph glands. The lungs and heart were normal; the pulse rate was 130 with good volume. The abdomen was normal. The reflexes were sluggish. The skin sensations were slightly hyperexcitable. The urine was normal. The white blood cells numbered 18,000. The Pirquet test was negative. Recovery was complete after two months.

SKIN REACTIONS OF PATIENTS WITH RHEUMATIC FEVER TO TOXIC FILTRATES OF STREPTOCOCCUS*

HOMER F. SWIFT, M.D.

MAY G. WILSON, M.D.

AND

E. W. TODD, M.D., D.P.H.

Rockefeller Medical Fellow

NEW YORK

Within recent years, the development of knowledge concerning the capacity for many strains of hemolytic streptococci to produce in broth cultures a substance which has certain resemblances to a soluble bacterial toxin has opened the field for study of a similar substance in other forms of streptococci. Following the discovery by Small [1] and Birkhaug [2] of indifferent streptococci in blood cultures of some patients with rheumatic fever, the latter observer investigated the capacity of these peculiar cocci to produce this kind of toxic filtrate, and he found that a much higher proportion of indifferent strains produced such toxic filtrates than did green streptococci. He also found that persons who had suffered from rheumatic fever were more susceptible to intracutaneous injections with these toxic filtrates than were other groups of persons, and consequently suggested that these micro-organisms might be the specific etiologic agents in this disease. Later, Kaiser [3] reported a study of the skin reaction of a much larger number of children who had had rheumatic fever and confirmed Birkhaug's original observations. In this study, however, a report was not made of the capacity of these children to react to boiled filtrate; and while a comparison of their reactions to the Schick and Dick tests is reported, study of a toxic filtrate of green streptococci is not recorded.

Because of finding green streptococci in the blood or lesions of patients with rheumatic fever by a number of observers, it seemed to us that the study of skin reactivity to toxic filtrates of various streptococci warranted more extensive investigation; hence the present work was undertaken.

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* From the Department of Pediatrics, Cornell University Medical College; the New York Nursery and Child's Hospital, and the Hospital of the Rockefeller Institute for Medical Research.

1. Small, J. C.: Am. J. M. Sc. **173**:101, 1927.

2. Birkhaug, K. E.: J. Infect. Dis. **40**:549, 1927.

3. Kaiser, A. D.: J. Infect. Dis. **42**:25, 1928.

MATERIAL AND METHODS

The clinical material consisted of children with rheumatic heart disease who had been under observation for several years in the wards and outpatient department of the New York Nursery and Child's Hospital, children with similar disease who were inmates of the Irvington Convalescent Home, and patients with active rheumatic fever in the wards of the Hospital of the Rockefeller Institute. In this material were included practically all of the usual manifestations of rheumatic fever: active and latent cases and cases in which recovery probably occurred were represented. Data on control cases were obtained from other departments of these institutions.

As a standard toxic filtrate, we used a preparation furnished us by Dr. Birkhaug. It was a ten-day filtrate in Douglas tryptic broth of strain RF1B. We attempted to prepare similar filtrates from a number of strains of indifferent streptococci including RF1B, but were unable to obtain solutions that gave as uniformly satisfactory reactions even though heavy growths of the bacteria occurred in the broth. It was evident, however, that different strains varied greatly in their capacity to produce "toxins," for different strains incubated under identical conditions produced solutions of varying strength. It seemed, therefore, that because satisfactory filtrates were obtainable from only selected strains of indifferent streptococci, it might be possible to obtain good "toxin" producers among some strains of green streptococci. We had in the laboratory strains V110A, isolated from a subcutaneous rheumatic nodule, and P63, which was isolated in pure culture from an apical abscess of a tooth extracted from a patient with nodules; both of them produced fairly satisfactory toxic filtrates—in fact, filtrates as good as any we were able to produce from indifferent streptococci. During the course of this work, Dr. Birkhaug informed us that better filtrates resulted from cultures incubated for from ten to twelve days than from those incubated six days. We were able to confirm his statement, and this suggested that the differences in the strength of the filtrates of the various streptococci might be due in part to differences in time of death and ease of autolysis. Zinsser and Grinnell [4] asserted that the allergizing substance from many bacteria is a result of a peculiar type of autolysis. We soon found that indifferent streptococci died much sooner in tryptic broth cultures than did green streptococci, and that films made on successive days showed an increasing number of gram-negative and involution forms. In some previous work it was found that autolysis of green streptococci was difficult to obtain. Hitchcock,[5] moreover, determined that most strains of indifferent streptococci easily underwent dissolution in sodium hydrate. We were also able to observe autolysis of indifferent streptococci incubated in salt solution for two weeks; such autolysates, when filtered, however, did not give as good skin reactions as were obtained with simple broth filtrates and were therefore not used extensively.

The broth filtrates were diluted to the desired strength with normal salt containing 0.5 per cent phenol. In most of the work fresh dilutions were made each week, but in the latter part, dilutions two or three weeks old were employed because

4. Zinsser, H., and Grinnell, F. B.: J. Bact. **14**:401, 1927.
5. Hitchcock, C. H.: J. Exper. Med. **48**:393, 1928.

it was found that they did not deteriorate in this period. Using tuberculin syringes and fine needles, we made injections of 0.1 cc. of the given dilutions into the skin of the mesial surface of the forearm or arm. The lesions were measured with a special outside adjusting caliper, as shown in figure 1, and the two longest diameters recorded in millimeters. In most instances the lesions were round or only slightly elliptic; hence, for purposes of comparison the sum of the two measured diameters was divided by 2, which gives the average diameter of a lesion. By recording the actual size of the lesion in this manner, all subjective impressions as to size, which are usually recorded by a different number of plus marks, were eliminated, and it was possible to compare accurately the results obtained in patients in different

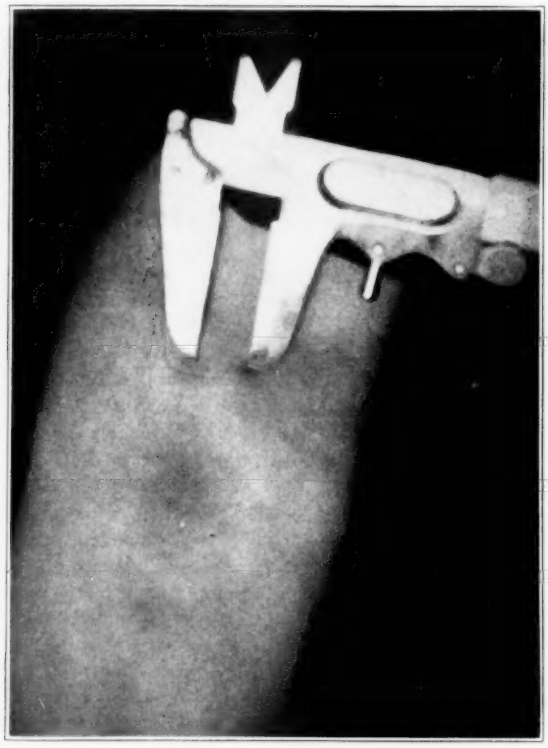

Fig. 1.—Type of outside diameter-caliper used to measure lesions.

institutions by different observers. The lesions in patients from the wards were measured every twenty-four hours for three days and those in patients from the outpatient clinic only after twenty-four hours, as it was found from the first group that the maximum size was attained in this period.

As many patients in the active stages of the disease were under the influence of drugs, it became desirable to determine their effect on the reactions. Two patients showing lesions with diameters of 14 and 15 mm., respectively, to a 1:100 dilution were given full therapeutic doses of sodium salicylate or neocinchophen for three days and then retested; the second reactions were of practically the same intensity as the first. As other patients under the influence of

these drugs seemed to give as strong reactions as would be expected, it was felt that this medication had little if any influence on the reacting capacity of the patient.

It soon became evident that the best RF1B filtrates furnished us by Dr. Birkhaug did not give reactions in nearly so high a proportion of active forms of the disease as reported by him and Kaiser. In fact, three fourths of our patients gave negative reactions with 1:100 dilutions; hence it became necessary to use 1:50 and 1:10 dilutions throughout the study. Generally, the test dose was 1:50, with a comparison of 1:10 or 1:100 in many patients. In a number of children, it was impractical to make many injections; hence a complete comparison could not be carried out in all cases. In most instances, a control injection of filtrate boiled for one hour was used. Birkhaug stated in his original communication that inactivation of the filtrate was brought about by this treatment; our observations on this point will be discussed later.

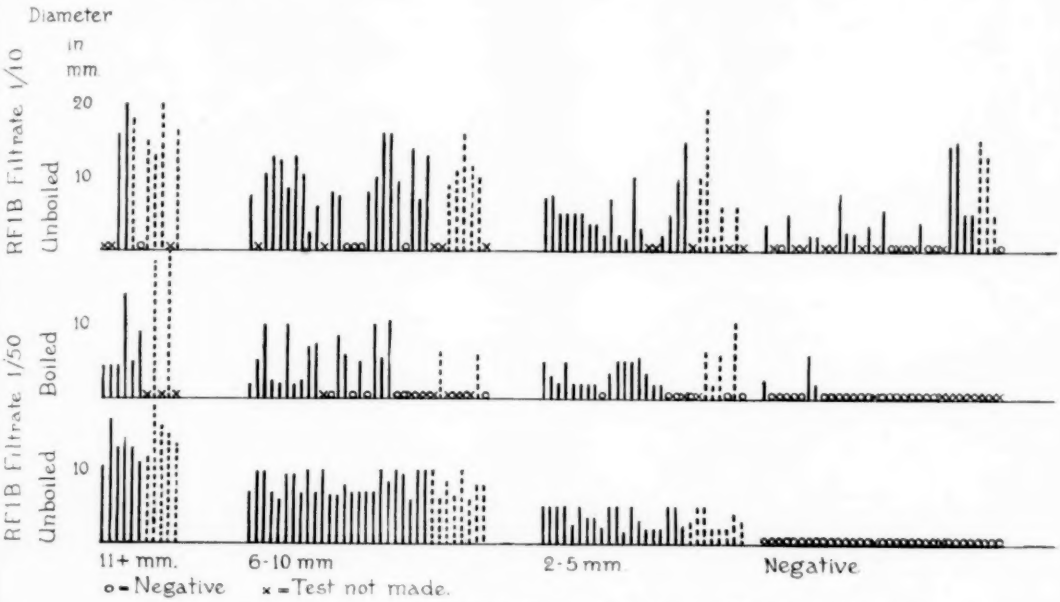

Fig. 2.—Skin reactions with RF1B filtrate in patients with rheumatic fever. O indicates negative and x, test not made.

RESULTS

The reactions obtained on first test of 105 patients with rheumatic fever with 1:50 dilution of filtrate RF1B is given in figure 2; all of these patients were also tested with either boiled filtrate of the same dilution or with unboiled filtrate in 1:10 dilution and most of them with both. The actual average diameter of each lesion is registered; in patients with active disease, the line is broken; in those in whom it was thought to be latent or cured, it is solid. Among this group of patients only 10 per cent gave a reaction of 11 mm. or more in the

area tested with the 1 : 50 dilution, while 31 per cent showed lesions of from 6 to 10 mm. Thus, less than one half of the entire group gave positive reactions with this dilution. When tested with 1 : 10 dilutions, about one-third showed lesions of 11 mm. or larger and one-fifth, lesions between 6 and 10 mm. In table 1 are given the figures for

TABLE 1.—*Reactions on First Test of Patients with Rheumatic Fever*

Size of Lesions	Active Rheumatic Fever No.	%	Inactive Rheumatic Fever No.	%	Combined No.	%
1 : 50 Dilution						
11 + mm.	5	19	6	7	11	10
From 6 to 10 mm.	8	31	25	28	33	28
From 2 to 5 mm.	8	31	20	22	28	24
0	5	19	39	43	44	38
Total	26		90		116	
1 : 10 Dilution						
11 + mm.	12	57	15	22	27	30
From 6 to 10 mm.	3	14	19	28	22	24
From 2 to 5 mm.	2	10	21	31	23	26
0	4	19	13	19	17	20
Total	21		68		89	
Controls						
1 : 50 Dilution						
Size of Lesions	Other Diseases No.	%	No Disease No.	%	Combined No.	%
11 + mm.	8	20	0	0	8	13
From 6 to 10 mm.	3	7	4	20	7	12
From 2 to 5 mm.	5	13	5	25	10	17
0	23	60	11	55	34	58
Total	39		20		59	
1 : 10 Dilution						
11 + mm.	10	20	5	20	15	20
From 6 to 10 mm.	8	16	3	6	11	15
From 2 to 5 mm.	8	16	3	6	11	15
0	23	48	15	68	38	50
Total	49		26		75	

these and a few additional cases together with a control group. These do not include retests, for it seemed that repeated injections increased the patients' sensitiveness in some instances.

It is important to establish some standard as to the size of lesion which shall be considered positive, and this can be done only by comparing the reactions of different groups of persons to various solutions. Some observers think that lesions less than 10 mm. in diameter should not be considered positive. We have, however, made somewhat differ-

ent classes, as shown in the table. If we include as positive only those of 11 mm. or more, only one fifth of the patients with active rheumatic fever gave positive reactions with 1 : 50 dilutions; but nearly two thirds of them gave positive reactions with 1 : 10 dilutions. Patients with inactive disease, on the other hand, showed lesions 11 mm. or larger in almost the same proportion as did nonrheumatic controls. If lesions 6 mm. or larger are included as positive, all categories among the patients with rheumatic fever are increased in considerably higher proportion than among nonrheumatic controls. As only one among twenty-five rheumatic patients showed a lesion of 6 mm. or more with a 1 : 10 dilution of broth, it seems justifiable to use this figure of 6 mm. as the lower limit of positive reaction, with the reservation that these smaller lesions are designated as only weakly positive. The important point brought out by this part of the study is that patients with active

TABLE 2.—*Effect of Heating Filtrate in Various Groups of Patients*

	Active Rheumatic Fever			Inactive Rheumatic Fever	Nonrheumatic	
	RF1B	P63	RF1B	RF1B	RF1B	RF1B
Dilution	1/10	1/10	1/50	1/50	1/50	1/10
Negative	0	1	....	19	10	7
Positive, unchanged	1 = 6%	1 = 10%	1 = 11%	14 = 22%	2 = 12%	0
Positive, became stronger	11 = 61%	8 = 80%	6 = 66%	14 = 22%	6 = 35%	3 = 60%
Positive, became weaker	6 = 33%	1 = 10%	2 = 22%	35 = 56%	9 = 53%	2 = 40%

rheumatic fever gave a much higher proportion of positive reactions than did those in whom the disease had become quiescent, and that a considerable number of patients with other diseases also gave positive reactions, although the latter group did not show as high a percentage of positive reactors as occurred among the rheumatic patients.

Reference to figure 2 also shows that patients sometimes gave as strong reactions with 1 : 50 dilutions as with 1 : 10 and occasionally gave negative reactions with the stronger dilution but positive reactions with 1 : 50. Another point is that in the majority of instances the "toxin" was not inactivated by boiling for one hour. The latter point was specially studied in a number of patients who were known to be positive reactors as well as in a number who were tested for the first time. In these patients, the unheated and boiled filtrates were injected on the same day. A summary of the results is shown in table 2.

The interesting point brought out by separating the patients into groups is that in the majority of those with active rheumatic fever the heated filtrate gave stronger reactions than did the unheated, while in

those in whom the disease was thought to be inactive and in the nonrheumatic patients the results were almost reversed, and in the larger proportion of cases the heated filtrate gave weaker reactions. Among most of these patients, however, the reaction did not become entirely negative. That increasing the toxicity of the filtrate by boiling was not a peculiar feature of that obtained from RF1B streptococci is shown in the second column of the table; strain P63, a typical *Streptococcus viridans*, with still other strains showed similar increase in toxicity.

A more detailed experiment to determine the effect of heating in various ways was then performed.

TABLE 3.—*Reactions of Patients to Filtrates Heated in Different Manners* *

		RF1B 1 : 10				P63 1 : 10			
		Unheated	Boiled 1 Hr.	Boiled 2 Hrs.	Autoclaved 15 Min.	Unheated	Boiled 1 Hr.	Boiled 2 Hrs.	Autoclaved 15 Min.
1	R. F.†	7	8	5	j.v.‡	6	7	4	j.v.
2	R. F.	14	17	5	19	5	7	5	6
3	R. F.	16	22	13	21	10	10	5	4
4	R. F.	19	22	15	19	0	0	0	0
5	R. F.	18	18	7	9	4	6	6	5
6	R. F.	20	22	19	17	6	6	5	5
7	R. F.	14	18	5	13	6	11	5	9
8	R. F.	11	13	0	11	0	5	6	7
9	Cardiac	0	0	0	0	0	0	0	0
10	Cardionephritic	24	28	22	24	0	0	0	0
11	Normal	22	26	16	18	6	7	4	4
12	Normal	15	17	8	11	7	7	8	9
13	Normal	0	0	0	0	0	0	0	0

* The figures indicate the diameter in millimeters.
† R. F., rheumatic fever.
‡ j. v., just visible.

One cubic centimeter of RF1B filtrate was placed in each of three glass tubes, which were then sealed by fusing the open ends. One was boiled for one hour in a water bath, the second for two hours, and the third was autoclaved at 118 C. for fifteen minutes. Three tubes of P63 filtrate were treated in the same manner. The tubes were then opened, all filtrates were diluted in the proportion of 1 : 10 with physiologic sodium chloride solution; unheated control filtrate was diluted in the same manner, and thirteen persons were each tested with the eight solutions. The measurements of the lesions twenty-four hours later are shown in table 3.

An interesting immediate reaction was noted in most of the persons tested. This consisted of a rapid enlargement of the wheal produced by the injection of the RF1B filtrate boiled for two hours; in practically all instances, there was a red aureola from 5 to 20 mm. wide surrounding the wheal. In some of the patients with rheumatic fever, a similar but less marked reaction was noted about the area tested with the P63 filtrate boiled for two hours; but this was practically absent in all of the controls. Thus, it appears that the filtrates, instead of being made less active by boiling, were made more toxic, so that two hours' boiling made them immediately toxic to very sensitive persons such as are found especially in a group

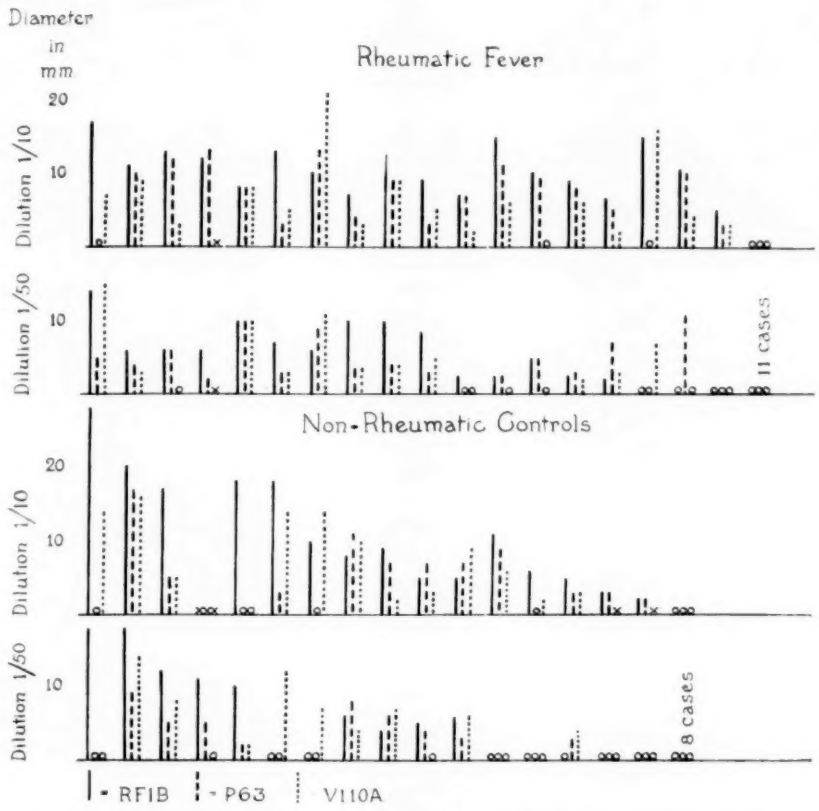

Fig. 3.—Comparison of skin reactions with RF1B, P63 and V110A filtrates. The solid line indicates RF1B; the broken line, P63 and the dotted line, V110A.

TABLE 4.—*Comparison of Lesions Produced by Three Different Filtrates*

	Rheumatic Fever—All Types			Nonrheumatic		
1 : 50 Dilution	RF1B	P63	V110A	RF1B	P63	V110A
11 + mm.	1	1	2	4	0	2
From 6 to 10 mm.	8	5	2	2	3	4
From 2 to 5 mm.	6	9	8	3	6	3
0.	14	14	17	15	15	15
No test	..	..	..	..	..	..
1 : 10 Dilution						
11 + mm.	9	4	2	6	2	4
From 6 to 10 mm.	8	8	6	4	4	3
From 2 to 5 mm.	1	5	8	5	5	5
0.	10	12	10	8	12	9
No test	0	0	1	1	1	3

of patients suffering from rheumatic fever. In practically all patients, the filtrates boiled for one hour gave larger lesions than did the control filtrates; in most of the patients, those boiled for two hours showed smaller lesions than did the controls at the end of twenty-four hours; the lesions from the autoclaved filtrates were variable. *Streptococcus viridans* P63 filtrate was less active than the RF1B filtrate in all cases. Case 10 is noteworthy: About six weeks before this test the patient, a man, suffered from an acute pyrexia lasting several days, and an intense infiltrated erythema of the thigh; and from his blood, *Streptococcus viridans* was grown in pure culture. After a few days' illness, he recovered and blood cultures were sterile. Thus, a patient known to have suffered a recent infection with *Streptococcus viridans* gave the most marked reactions with filtrate from indifferent streptococci. Case 12 is also noteworthy; the patient, a normal control, is known to be sensitive to filtrates of some hemolytic streptococci, but on a previous occasion gave negative reactions with 1:100 RF1B filtrate. He has, moreover, been repeatedly tested with various hemolytic streptococcus filtrates, and possibly is being made more and more sensitive by this treatment.

Some rabbits which had been made hypersensitive by means of repeated intracutaneous inoculations with *Streptococcus viridans* V110A were found to give well marked reactions to 1:10 dilutions of RF1B filtrate. Thus, by direct experiment, it was shown that there was a crossing of the hypersensitive state with respect to both green and indifferent streptococci, and that in such hypersensitiveness boiling of the toxic filtrate did not render it inactive. As far as the skin test is applicable, therefore, it seems that the hypersensitiveness of these animals and that of many of the patients tested is comparable.

After the work had progressed a certain distance, it became evident that persons in both the rheumatic fever and control group at times gave positive reactions with filtrates from some strains of *Streptococcus viridans*. The most potent strains were P63 and V110A. From them twelve-day filtrates were prepared and a series of comparative tests made with strain RF1B. In most cases, the three unheated filtrates were used in both 1:50 and 1:10 strength. About one half of the patients had been tested previously. The results are recorded graphically in figure 3, in which the average diameters of the lesions obtained with the three filtrates are placed side by side to render comparison easy. The figures are summarized in table 4. A study of these two shows that many patients who were sensitive to filtrates from indifferent streptococci were also sensitive to filtrates from *Streptococcus viridans*. It is true that the filtrate from the former gave a higher proportion of positive reactions than from the latter in patients with rheumatic fever, but this was also the case in the nonrheumatic controls. The groups are hardly large enough for statistical comparison; they merely bring out the fact that type specificity in respect of either strain did not exist in either group of persons.

After some patients had been retested two or three times, it was noted that reactions were positive with dilutions of toxic filtrate that previously had given only negative results. In a small series of patients who were retested with either 1:10 or 1:50 dilution of filtrate RF1B,

the results are shown in figure 4. The 1 : 10 dilution is indicated by the broken line and the 1 : 50 dilution by the solid line. All of these patients were retested within a period of five weeks. The summary of these results, shown in table 5, indicates that in the majority the weaker dilution gave a stronger reaction at the time of second testing than at the first. In eight patients retested after a period of three months or more with this weaker dilution, only three showed a slight increase

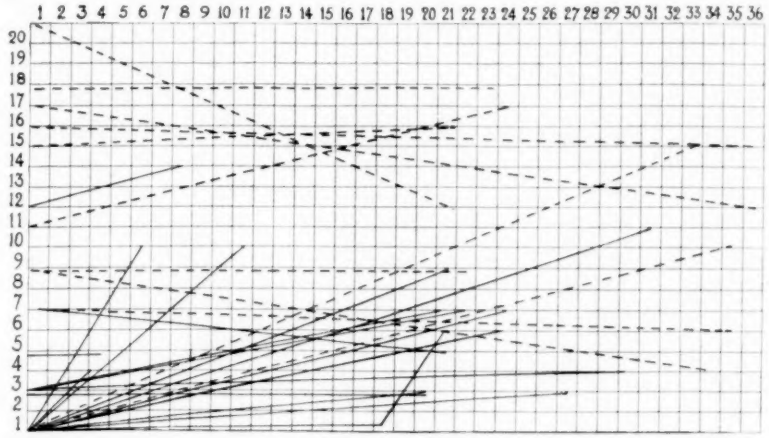

Fig. 4.—Variation in size of skin reactions on repeated tests. The solid line indicates 1 : 50 dilution, and the broken line, 1 : 10 dilution of RF1B filtrate.

TABLE 5.—*Effects of Retesting Within Period of Five Weeks*

	1 : 10 Dilution	1 : 50 Dilution
Increase	4	11
Decrease	5	1
Same	2	2
Always negative	3	2
Total	13	16

in strength of reaction. At the time of the first testing most of the patients had received from four to six intracutaneous injections of various dilutions of toxic filtrate. The charted results suggest that patients already somewhat sensitive to such filtrates may at times have their skin sensitiveness increased by these injections. As Birkhaug was able to render himself highly hypersensitive to a filtrate by repeated injections, such a suggestion does not appear unreasonable. These observations indicate at least that for purposes of comparing the skin reactivity of various groups of persons the first test should be the one to be recorded, and a period of from eight to ten weeks should probably elapse before retesting.

The distribution of patients according to age groups is shown in table 6. Unfortunately, the number of patients in the various categories varies so much that comparisons are of little value. Especially is this true when patients with rheumatic fever are compared with nonrheumatic persons. Among the former the proportion of positive reactors increased with advancing years; while among the latter, the figures were more variable, doubtless due to the small number of cases in most groups. To be of value, a study of this point should, however, contain groups of approximately the same size distributed among rheumatic, nonrheumatic and apparently normal persons. It is possible that prolonged infection of the upper respiratory tract, such as tonsillitis or chronic sinusitis, diseases that are often encountered in connection with rheumatic fever, may be the factor determining the induction of this type of hypersensitiveness.

TABLE 6.—*Proportion of Hypersensitive Individuals in Various Age Groups*

	Rheumatic Fever			Nonrheumatic Fever		
Age	Number	+	Per Cent	Number	+	Per Cent
3 or under.....	0	0	0	18	5	28
From 4 to 6.....	4	0	0	5	3	60
From 7 to 9.....	20	9	45	7	1	14
From 10 to 12.....	43	24	56	6	2	33
From 13 to 15.....	23	13	56	7	1	14
16 + ...	14	9	64	35	12	34

It seemed desirable to determine the reaction of a group of patients with rheumatic fever to a filtrate of hemolytic streptococci; and as the toxin from *Streptococcus scarlatinae* has been so extensively used in the Dick test, this was chosen for comparison. Among 112 patients with either active or latent rheumatic fever, 15 showed positive reactions. In 3 others there were negative or faintly positive reactions with unheated toxin but strongly positive reactions with boiled toxin. In 41 patients in whom the Dick test was compared on the same day with their reactions to RF1B filtrate in a dilution of 1:50, the results were as follows: positive to RF1B filtrate and positive to the Dick test, 2; positive to RF1B filtrate and negative to the Dick test, 17; negative to RF1B filtrate and positive to the Dick test, 4; negative to RF1B filtrate and negative to the Dick test, 18. These figures indicate that there was no distinct relationship in the patients' capacity to react to the two types of filtrates. Indeed, the Dick reactions were distributed much the same as would have been expected in any unselected group of children.

COMMENT

While the number of patients tested during this investigation was not so large as that reported by Kaiser, nevertheless it contained representatives of all phases of rheumatic fever and enough controls to indicate at least the significance of these reactions and the type of hypersensitiveness elicited by these tests. There is an additional advantage resting in the fact that they were our own patients and had been studied most carefully from various angles.

The reactions obtained with these filtrates closely resemble those obtained with tuberculin. While there was some local redness within a few hours of the time of injection, the most marked reaction usually occurred about twenty-four hours later. In strong reactors there was distinct brawny infiltration of a dull red and in weak reactors only an intense erythema with little if any palpable infiltration. The filtrate was increased in potency by prolonged incubation of the broth culture. It seemed to be easier to obtain potent filtrates from indifferent streptococci than from green forming strains, although good filtrates were sometimes obtainable from the latter types. As indifferent strains die out much sooner when incubated in broth than do green forming strains and undergo autolysis more readily, it is suggested that the toxis substance is set free from the bodies of the micro-organism as they break up. Mackenzie and Hangar [6] found a "toxin" in certain strains of both green and hemolytic streptococci, but stated that it was rapidly destroyed if the incubation of the culture was continued for forty-eight hours. They also found that many strains rapidly lost their "toxin" producing capacity on repeated subcultures on an artificial medium. In their tests the filtrates were used undiluted; hence their results cannot be closely compared with ours. In one respect, however, we agree: the reactions are not strictly specific for rheumatic fever, because when filtrates are used in sufficient strength to give a reaction in the majority of patients with rheumatic fever, they also give reactions in a smaller proportion, but still in a fair number, of patients with other diseases. This is not surprising when we consider the ubiquity of streptococci in the respiratory tract and how frequently they can be recovered from deep in the tonsils, from the paranasal sinuses and from apical abscesses.

Hitchcock [7] has shown that the incidence of indifferent streptococci in the throats of patients with rheumatic fever is no greater than in the throats of other patients. Their ability to produce toxic filtrates seems to rest in some peculiarity of this type of micro-organism rather than

6. Mackenzie, G. M., and Hangar, F. M., Jr.: J. Immunol. **13:** 41, 1927.
7. Hitchcock, C. H.: J. Exper. Med. **48:**403, 1928.

in a special specific etiologic rôle in respect of rheumatic fever. It is true that patients with active rheumatic fever show reactions with such filtrates in a greater percentage of instances than do normal persons or persons with other diseases; but this seems to be due to a condition of much increased hypersensitiveness of these patients, for they show a similar hypersensitiveness to filtrates from certain green streptococci. Derick, Hitchcock and one of us (H. F. S.) [8] moreover, have demonstrated marked hypersensitiveness of many of these patients to nucleoproteins prepared from all types of streptococci but most marked to those from hemolytic types. In some patients with weak or negative reactions with filtrates of indifferent streptococci, there were marked reactions with such nucleoproteins.

Another feature of the hypersensitiveness of many patients with rheumatic fever is that when they are tested with boiled filtrate stronger reactions are often elicited than when they are tested with unheated solutions. Most patients with inactive or "cured" rheumatic fever, on the other hand, show less marked reactions with boiled filtrate. While this was not the universal rule in our patients, we were always faced with the difficulty of determining whether or not the disease was inactive. Often there is a low grade persistent infection that permits of correct interpretation only after years of observation. But this difference of reactivity in the two classes of patients with rheumatic fever is noteworthy and possibly explains the discordance in the results obtained by us and by Birkhaug and Kaiser. Unfortunately, they did not report the clinical condition of their patients; but it is evident from Kaiser's report that the majority of his patients were in the class designated by us as inactive.

Birkhaug reported that he was able to neutralize the soluble toxin RF1B with an antitoxic serum. He sent us a small amount of this serum; but in a few patients with active rheumatic fever and in some others with strong skin reactions, we were unable to obtain any evidence of neutralization. Some of these patients, on the other hand, showed stronger reaction with the mixture of serum and filtrate than with either alone. We did not carry out enough neutralization experiments to control all phases of the question, but suggest that in this respect there may also be a difference between a patient with active disease and one in the latent stages. Some rabbits which were made hypersensitive to green streptococci and which gave positive reactions with filtrate RF1B also failed to show any neutralization of this toxic filtrate with this antitoxic serum. Mackie and McLachlan [9] sensitized

8. Swift, H. F.; Derick, C. L., and Hitchcock, C. H.: Tr. A. Am. Phys., 1928, vol. 43, to be published.

9. Mackie, T. J., and McLachlan, D. G. S.: Brit. J. Exper. Path. **8**:129, 1927.

guinea-pigs with living cultures of *Streptococcus scarlatinae* and observed that it was impossible to obtain neutralization of skin reactions with antitoxic serum, and also that heating of the toxic filtrate often did not inactivate it. Some of their animals were also sensitive to filtrates of green streptococci. Zinsser and Grinnell [10] had previously had somewhat similar experiences in regard to sensitization of animals with streptococci from patients with scarlet fever. It is evident from the work of Dochez and Stevens [11] that at least two types of hypersensitiveness to streptococci do exist: one to a toxic product which can be neutralized, and another, probably broader, to a streptococcus product which cannot be neutralized. Because of the number of different strains and products of streptococci to which patients with rheumatic fever react, we are inclined to believe that they have the second type of hypersensitiveness; and that it is the hypersensitiveness of the patient suffering from rheumatic fever rather than the specificity of the toxic filtrate of streptococci which explains the peculiarity of the phenomena observed when these two are brought into contact as in the skin test.[12]

SUMMARY

Patients with rheumatic fever gave a higher proportion of positive skin reactions with filtrates of both indifferent and green streptococci than did nonrheumatic controls.

Patients with active rheumatic fever gave a higher proportion of skin reactions with these filtrates than did those with inactive or "cured" rheumatic fever.

When the reactions with unheated filtrate were compared with those with filtrate boiled one hour it was found that the boiled filtrate gave stronger reactions in most patients with active rheumatic fever and weaker reactions in most patients with inactive or "cured" rheumatic fever.

A close correspondence was not found in the capacity of patients to give skin reactions with Dick "toxin" and filtrates of nonhemolytic streptococci.

Positive reactions in patients with rheumatic fever seem to depend more on the state of hypersensitiveness to certain products of streptococci than on the specificity of any one type of streptococcus.

10. Zinsser, H., and Grinnell, F. B.: J. Immunol. **10**:725, 1925.
11. Dochez, A. R., and Stevens, F. A.: J. Exper. Med. **46**:487, 1927.
12. See also Strauss, H.: Deutsche med. Wchnschr. **53**:737, 1927.

Case Reports

TRAUMATIC NECROSIS OF THE SUBCUTANEOUS FAT OF THE NEW-BORN INFANT*

LEON DE VEL, M.D.
WITH MICROSCOPIC REPORT BY
ZERA A. BOLIN, M.D.
SAN FRANCISCO

Though numerous papers have been written in Europe on traumatic necrosis of the subcutaneous fat of the new-born infant, and a great advance has been made recently as to the understanding of the etiologic factors of this condition, American literature on the subject is scarce.

In reviewing the literature, much difficulty was encountered because of the varying nomenclature and the incompleteness of data in a number of papers. In 1890, Holt, in discussing a paper by Northrup,[1] related a clinical history fitting in with the condition with which we are here concerned. In 1905, Sobel[2] reported a case under the name of sclerema neonatorum. Fabyan[3] was first to publish a clinical report with histologic observations, under the title "Disseminated Subcutaneous Fat Necrosis, Occuring in an Infant, Without Other Lesions." In 1923, Fabyan's paper was overlooked by Farr,[4] when he reported what he thought to be the first case of subcutaneous fat necrosis in an infant published in America. Lieberthal,[5] though lacking histologic data on his case, was first to point out the relation of the condition to obstetric trauma.[6]

We recently had the opportunity to make the following observations.

REPORT OF A CASE

History.—P. M., a white infant boy, was brought to the University of California Hospital outpatient department on March 27, 1928, at the age of 21 days.

* Received for publication, July 9, 1928.

* From the Department of Pediatrics, University of California Medical School.

1. Northrup, W. P.: Sclerema Neonatorum, Arch. Pediat. **17**:1, 1890.

2. Sobel, J.: Sclerema Neonatorum: Report of a Case with Recovery, Arch. Pediat. **22**:264, 1905.

3. Fabyan, M.: Disseminated Subcutaneous Fat Necrosis, Bull. Johns Hopkins Hosp. **18**:349, 1907.

4. Farr, C. E.: Ischemic Fat Necrosis, Ann. Surg. **77**:513, 1923.

5. Lieberthal, D.: Sclerema Neonatorum and Scleroderma, J. Cutan. Dis. **36**:29, 1918.

6. Gray, A. M. H.: Sclerema-Neonatorum, Arch. Derm. & Syph. **14**:635 (Dec.) 1926; Discussion of Cases of Harrison (footnote 14).

His mother brought him in primarily for feeding directions, having been referred from the Hospital as a follow-up case. She said that the infant was doing well. Indeed, on first glance, the patient looked to be a large, healthy new-born infant. He weighed 4,640 Gm. and was 55 cm. in length. On closer examination, however, several indurated areas were found in the skin.

Examination.—On the left side of the neck a ribbon-like induration of the skin was felt, which was about 6 mm. wide and which started under the chin slightly to the left of the midline, running parallel to the mandibular border, about 1.5 cm. below it, crossing the sternocleidomastoid muscle and passing into the posterior region of the neck, where it suddenly widened to a plaque about 4 cm. long and 2 cm. wide, reaching well beyond the midline toward the right side. This plaque was slightly raised above the level of the surrounding skin and had a peculiar red-purplish color. The borders of the indurated area were sharp and easily outlined. The whole area was freely movable over the underlying structures. A second plaque, about 1 cm. in diameter, presenting the same characteristics, but without discoloration, covered the area of the left mastoid. A third indurated zone, 2 by 1 cm., was lying over the crest of the left scapula. A fourth and fifth zone, 2 by 1 cm. and 1 by 1 cm., were found along the inner border of the left

TABLE 1.—*Pelvic and Fetal Measurements*

Pelvic Measurements		Fetal Measurements	
Interspinous distance	25.5 cm.	Weight	4,120 Gm.
Intercristal distance	26.5 cm.	Length	55 cm.
Intertrochanteric distance	31.5 cm.	Occipitomental diameter	15.5 cm.
Diameter of Baudelocque	21.0 cm.	Occipitofrontal diameter	13.5 cm.
Bi-ischial distance	9.5 cm.	Suboccipitobregmatic circumference	32.5 cm.
Diagonal conjugate	12.0 cm.	Circumference of shoulders	34.5 cm.

scapula. All the plaques were freely movable over the underlying tissues. All but the first were level with the surrounding skin and of normal color. Careful examination of the entire skin area did not reveal any other indurations. The results of the physical examination were otherwise entirely negative.

The following information concerning the birth of the child was obtained from the department of obstetrics.

History of Birth.—P. M., a woman, a primipara, aged 18, was delivered at term on March 6, 1928. The position was left occipito-anterior. Because of insufficient vis a tergo and threatened fetal exhaustion, low forceps (Keilland) were applied. The total duration of labor was twenty hours. The child appeared slightly asphyxiated, but responded quickly when friction was applied to the back. The caput was more marked to the left. There was a facial paralysis on the left side and an area of ecchymosis over the left side of the neck and the left mandible. The pelvic and fetal measurements were as follows:

The infant received a prophylactic intramuscular injection of 45 cc. of whole blood shortly after birth. The ecchymoses disappeared in a few days. The facial paralysis gradually subsided and had entirely disappeared by the eighth day. On the ninth day, slight respiratory stridor was noted, also short periods of mild cyanosis. An x-ray treatment was given over the thymus area, apparently without result. The infant weighed: 4,120 Gm. at birth, 3,850 Gm. the third day

(lowest) and 4,250 Gm. the fourteenth day (discharged). On the fourteenth day, the day of discharge from the hospital, "several small lumps" were noted on the left side of the neck.

Further Observation.—On March 30, at the age of 24 days, the infant had had a convulsive seizure involving the left side of the face and the left arm and leg. New indurations of the skin had not appeared, and the ones already described had not changed.

On March 31, the infant was admitted to the University of California Hospital. He had had several more left-sided clonic convulsions. There was no fever. Lumbar puncture revealed yellowish-pink fluid under slightly increased pressure, containing 510 red cells per cubic millimeter, mostly crenated. The Pandy test was positive. The colloidal gold curve was: 0001221100. The Wassermann reaction was negative. Cultures were sterile. The examination of the blood showed: red blood cells, 5,590,000; hemoglobin, 90 per cent, Tallqvist; and the white blood cells, 12,600. The coagulation time was three minutes.

On April 2, there had not been a recurrence of the convulsions. X-ray examination of the neck failed to show calcification in the indurated areas. Intradermal tuberculin tests with 0.1 mg. of human and bovine types were negative.

On April 3, the spinal fluid was clear, with eight cells per cubic millimeter. The chemical analysis of the blood showed: nonprotein nitrogen, 40; chlorides, 585; cholesterol, 89; calcium, 11.,5 and phosporus, 3.4 mg. per hundred cubic centimeters.

On April 6, the convulsions had not recurred. The infant was thriving and weighed 4,860 Gm. There had not been a change in the number, size or character of the lesions of the skin. A specimen for biopsy was removed from the indurated plaque in the neck. The patient was discharged.

On April 9, the infant weighed 5,080 Gm. The lesions of the skin were unchanged. The small operative wound had healed by first intention.

On April 17, the infant weighed 5,480 Gm. He was 42 days of age. It was approximately the twenty-eighth day of the disease. The lesions of the skin began to show definite signs of regression; they were becoming smaller and the induration was less marked.

On May 2, the infant weighed 6,100 Gm. It was approximately the thirty-second day of the disease. The mastoid plaque and the three lesions around the scapula had entirely disappeared without leaving any trace. There was only a portion of the submaxillary cord the size of a pea left, and the large plaque in the neck had broken up into several small fragments.

On May 15, all the lesions had entirely disappeared without leaving a trace. The x-ray examination failed to reveal calcification.

Pathologic Report on Biopsy Material (Bolin).—The specimen consisted of biopsy of the skin and subcutaneous tissue from the neck.

Microscopic examination showed the skin to be normal. Below the skin and disconnected from it, there was a mass of tissue which was seen to lie in the fat. At the bottom of the skin, there was a small portion of fascia. The fat showed normal lobulation separated by connective tissue. The connective tissue, however, was increased in amount. There was not any hemorrhage in the tissue, either new or old. There was not a sign of inflammatory reaction. The nodules in the fat were composed of a cellular tissue which replaced a large portion of each fat lobule. The fat cells themselves did not appear to be altered. The invading tissue consisted of cells of the macrophage type with rather large amounts of proto-

plasm and a small, moderately staining nucleus, and interspersed among these were a large number of giant cells. These cells were of foreign body type and showed places in the protoplasm from which some substance had been removed by the embedding process. In some of the spaces next to these giant cells there were seen needle-shaped spaces in the form of fans and rosets. Between this cellular tissue there was a moderate amount of new connective tissue. The blood vessels were normal.

Frozen sections made and examined with a polarizing microscope, both warm and cold, showed an occasional droplet which gave a double refraction with a cross, as seen in cholesterol.

Frozen sections stained with scarlet red showed that the fat globules stained up a brilliant orange red. The needle-shaped crystals did not take this stain, but remained more or less transparent. Frozen sections stained with nile blue showed that these crystals did not take this stain. From our examination, it is not possible to determine accurately the nature of these crystalline substances, but they probably are a mixture of cholesterol esters and fatty acid crystals.

The diagnosis of subcutaneous traumatic necrosis of fat was made.

COMMENT

In the French and German literature, the condition is variously called: scleroderma neonatorum, subkutane Fettgewebsnekrose, adiponecrosis subcutanea neonatorum, induration cutanée curable des nouveau nés, sclérème adipeux en plaques, cytostéatonécrose du tissu sous-cutané des nouveau nés; British authors prefer the term sclerema neonatorum.

CLINICAL COURSE

The majority of the lesions appear toward the end of the first and at the beginning of the second week, sometimes as early as the second day or as late as the third or fourth week. They occur mostly in large and heavy infants (Riesenkinder of Bernheim-Karrer[7]), in those born of elder primiparas, or after a hard or prolonged labor. The lesions are multiple, found on the cheeks, neck, back, shoulders, arms (deltoid area), buttocks and thighs, in those places that are particularly exposed to obstetric trauma. They vary greatly in size, from that of a pea to that of a palm of the hand or even larger. There is but little elevation above the level of the surrounding skin, often none. The color may or may not be abnormal, and is sometimes reddish or with a purple tinge. The borders are sharp and easily outlined by palpation. Their woodlike induration is striking, and when slight tangential pressure is exerted, the overlying skin shows the roughened aspect of orange peel. Occasionally, small cysts may form. There is no pain, either spontaneous or on pressure. Health and nutrition are unaffected and the temperature is

7. Bernheim-Karrer: Ueber subcutane Fettgewebsnekrosen beim Neugeborenen, Ztschr. f. Kinderh. **42**:658, 1926.

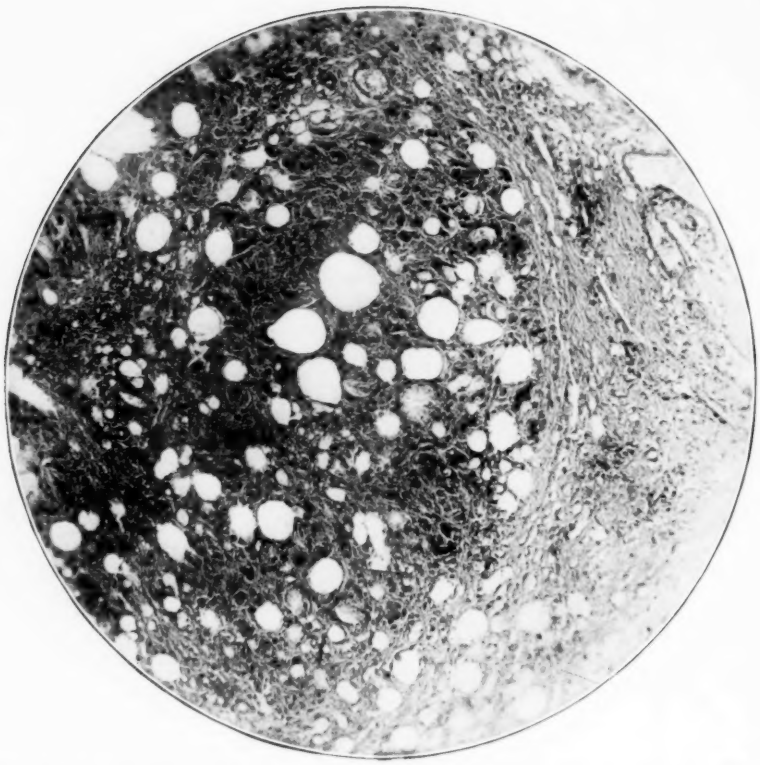

Fig. 1.—Low power view of chronic inflammatory reaction with fibrosis of fat, giant cells and fatty acid crystals.

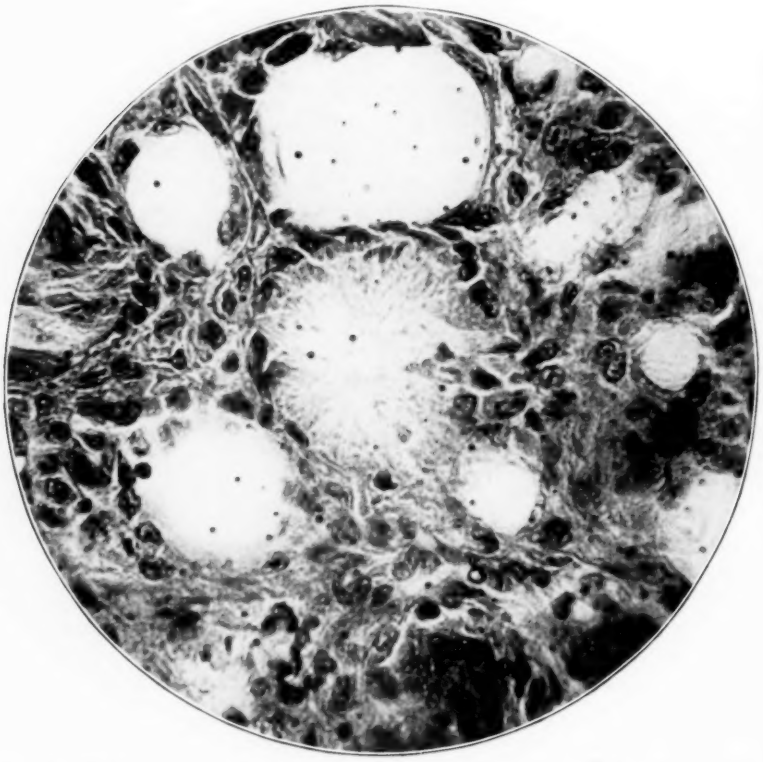

Fig. 2.—High power view of a portion of the central area of figure 1, showing detail of fatty acid crystals (empty linear spaces) and several giant cells.

normal. The lesions do not all appear at the same time; they soon reach their full development and remain stationary for several weeks or even months. Then regression begins and they disappear without leaving any trace. In only two instances has calcification of the skin been reported.

PATHOLOGY

Histologically, the fat lobules appear enlarged and infiltrated with large cellular elements. These cells increase in size and their greatly increased cytoplasm contains one, or more often, several nuclei. In frozen sections these large phagocytic cells often show elongated pointed crystals, frequently arranged in the form of a roset or fan. In paraffin sections the crystals have been dissolved out, but they appear as empty linear spaces. The abnormal fat and crystals act as a foreign body, and the infiltration with macrophages and the formation of foreign-body giant cells is an inflammatory reaction preliminary to resorption.

The first histologic description was given by Fabyan[3] in 1907. Subsequent reports by Triboulet, Ribadeau-Dumas and Debré,[8] Bernheim-Karrer,[9] Keilmann,[10] Farr,[11] Carol and van der Zande,[12] de Elizalde,[13] Harrison and McNee,[14] Woringer and Weiner,[15] are all singularly concordant as to the histologic conditions that characterize the disease.

ETIOLOGY

There is little doubt but that obstetric trauma is the etiologic agent. The mechanism is probably an ischemia of localized areas of the skin, by compression against harder underlying structures during passage through the birth canal, application of forceps or too vigorous attempts at revivification of an asphyxiated infant. As a result of this, changes take place in the fat. Chemical analyses by Schultz[16] show a palmitin-

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8. Triboulet, Ribadeau-Dumas and Debré: Sclérème adipeux en plaques, Bull. Soc. de pédiat. de Paris. **14**:199, 1912.

9. Bernheim-Karrer: Ueber subcutane Fettgewebsnekrosen beim Neugeborenen, Schweiz. med. Wchnschr. **3**:12, 1922, footnote 7.

10. Keilmann, K.: Circumscripte symmetrische Fettsklerose im Säuglingsalter, Ztschr. f. Kinderh. **33**:298, 1922.

11. Farr, C. E.: Ischemic Fat Necrosis, Ann. Surg. **77**:513, 1923.

12. Carol, W. L., and van der Zande, F.: Adiponecrosis subcutanea neonatorum, Nederl. Tijdschr. v. Geneesk. **69**:1317, 1925; Acta derm.-venereol. **7**:180, 1926.

13. de Elizalde, P.: Necrosis del tejido graso subcutaneo en el niño de pecho, Semana méd., 1923.

14. Harrison and McNee: Sclerema Neonatorum, Arch. Dis. Childhood **1**:63, 1926.

15. Woringer, P., and Weiner, G.: La cystostéatonécrose du tissu souscutané chez le nouveau-né, Rev. franç. de pédiat. **4**:57, 1927.

16. Schultz: Zentralbl. f. allg. Pathol. u. path. Anat. **35**:243, 1924.

stearin mixture, by Carol and van der Zande [12] cholesterol esters, by Harrison [14] neutral fats, by Smith [17] fatty acids, by Lecène and Moulonguet [18] soaps. Whatever the true chemical nature of the substance, it acts as a foreign body and sets up a chronic inflammation similar to that which occurs after the injection of petrolatum or paraffin.

To Lieberthal [5] belongs the credit of having first pointed out the etiologic influence of birth trauma. His views were later shared by Bernheim-Karrer,[9] Keilmann,[10] Voigt and Schultz,[19] Carol and van der Zande,[12] Woringer and Weiner,[15] Marfan and Hallez,[20] and Marfan and Debray.[21]

Arguments brought forth (particularly by Woringer and Weiner [15]) in favor of the theory of obstetric trauma are:

1. The difficulty of labor.
   (*a*) Because of the large size of the infant: all of Bernheim-Karrer's fourteen patients weighed over 3,500 Gm., seven over 4,000 Gm.; Lieberthal's weighed 4,190 Gm.; Voigt and Schultz's weighed 4,850 Gm.; Marfan's weighed 4,400 Gm.; Carol's weighed 4,000 Gm., and our patient weighed 4,120 Gm. at birth.
   (*b*) Because of difficulties on the part of the mother, such as primiparity in older women (Bernheim-Karrer's were all over 25 years of age), narrowness of the pelvic outlet, unusual resistance of the pelvic floor and the application of forceps. One case occurred after cesarean section, where the child was born asphyxiated and badly bruised.
2. The frequency with which one encounters other evidence of obstetric trauma: most of these infants are born asphyxiated, and cephalhematomas, paralyses and intracranial hemorrhage are frequently seen. Furthermore, the localization of the lesions is predominant in the more exposed areas of the skin; so far none has been described on the abdomen, or in the axillae or on the inner aspect of the thighs.

In older observations, weight, height and circumstances surrounding labor are often lacking. Table 2 summarizes the observations in selected, more completely reported cases.

In eleven of the thirty-three cases here tabulated, the infants weighed between 3,500 and 4,000 Gm., thirteen weighed 4,000 Gm. or more, and for three data are not given. Labor was precipitate in one of the thirty-three patients, difficult in twenty-two and normal in six. Data were not given for four.

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17. Smith, C. S.: J. Cutan. Dis. **36**:436, 1918.

18. Lecène, P., and Moulonguet: La cystostéatonécrose ou saponification intracellulaire du tissu cellulo-adipeux, Bull. d'anat. path. méd.-chir. **2**:193, 1925.

19. Voigt and Schultz: München. med. Wchnschr. **71**:845, 1924.

20. Marfan and Hallez: Induration cutanée curable des nouveau-nés, par nécrose traumatique du tissu cellulo-adipeux, Bull. Soc. de Pédiat. de Paris **24**: 56, 1926.

21. Marfan and Debray: Bull. Soc. de Pédiat. de Paris **24**:60, 1926.

There was other evidence of trauma at birth in twenty-three of the thirty-three cases. Data were not given in ten cases.

3. The striking similarity between the pathologic lesions of traumatic necrosis of the subcutaneous fat of the new-born infant and lesions of the skin found definitely in relation to trauma.

   (*a*) Traumatic fat necrosis of the female breast, as described by Lee and Adair,[22] Gottesman and Zemansky,[23] Farr,[11] Lecène and Moulonguet,[18] Sénèque,[24] Stulz and Fontaine,[25] in which there seems to be a definite traumatic factor.

   (*b*) Experimental traumatic fat necrosis, such as was carried out by Berner[26] and Heyde,[27] and by Farr,[11] who produced the pathologic lesion of fat necrosis by pinching the skin of young pigs with forceps.

TABLE 2.—*Observations in Selected, Completely Reported Cases*

Author	Cases	Weight, Gm.	Length, Cm.	Labor	Trauma
Cruse: Jahrb. f. Kinderh. **13**: 35, 1879	I	3,340	..	No data	No data
	III	3,150	50	No data	No data
	IV	4,350	51	No data	Asphyxia
Sobel [2]	1	2,720	..	Precipitate	Asphyxia
Fabyan [3]	1	2,970	46	Normal	Asphyxia
Paterson: Quart. J. Med. **18**: 317, 1915	1	3,680	..	Normal	Cyanosis, convulsions
Morquio: Arch. latino-am. de pediat., 1915	1	.....	..	Forceps	No data
Lieberthal [5]	1	4,190	..	Normal	No data
Pollitzer: Riv. di clin. pediat., 1921, p. 435	1	3,500	..	Normal	No data
Farr [11]	1	.....	..	Forceps	Brachial palsy
Voigt [19]	1	4,850	..	Prolonged transverse	No data
Carol [12]	1	4,000	..	Prolonged	Asphyxia, flagellation
Harrison [14]	III	3,900	..	Normal	No data
	IV	.....	..	No data	Asphyxia, cyanosis
	V	3,180	..	Normal	"Fits and blue turns"
Bernheim [9]	7	3,500+	..	{13 primiparas	11 asphyxiated
	7	3,000+	..	{14 over 25	7 other trauma
Marfan [20]	1	3,400	..	Forceps	Asphyxia, flagellation
Marfan [21]	1	4,400	..	Forceps	Hematoma, palsy, fracture
Woringer [15]	1	3,500	..	Difficult,	Asphyxia
Author's case	1	4,120	55	Forceps	Asphyxia, palsy, intracranial hemorrhage

DIAGNOSIS

Traumatic necrosis of the subcutaneous fat of the new-born infant has nothing in common with scleroderma. The pathologic processes are totally different: fat necrosis is opposed to hypertrophy of connective

22. Lee, B. J., and Adair, F. E.: Traumatic Fat Necrosis of the Female Breast, Ann. Surg. **72**:188, 1920; Surg. Gynec. Obst. **34**:521 (April) 1922; Ann. Surg. **85**:670, 1924.

23. Gottesman and Zemansky: Fat Necrosis of the Female Breast, Ann. Surg. **85**:513, 1923.

24. Sénèque, M.: Bull. Soc. Nat. de Chir. **52**:697, 1926.

25. Stulz, E., and Fontaine, R.: Rev. de chir. **61**:646, 1923.

26. Berner: Virchows Arch. f. path. Anat. **193**:510, 1908.

27. Heyde, M.: Deutsche Ztschr. f. Chir. **109**:500, 1911.

tissue followed by atrophy of the epidermis.[28] The clinical picture is also different. The name "scleroderma" should therefore not be applied to the condition here described.

Sclerema neonatorum is a misleading term. It implies a different clinical picture (occurs in premature, debilitated "foundlings," starts on the lower extremities and gradually spreads upward), a different pathologic picture on which investigators do not seem to agree and a bad prognosis. Further clinical and pathologic study of such cases is desirable.

Traumatic necrosis of the subcutaneous fat of the new-born infant is a definite clinical entity, occurring as the result of trauma and presenting a well defined microscopic picture. It should not be called by any other name.

TREATMENT AND PROGNOSIS

The prognosis of traumatic necrosis of the subcutaneous fat of the new-born infant is good. The lesions do not cause any disturbance and disappear without leaving a trace. Calcification as reported in two of Harrison's cases has not been reported in any other case. Treatment is not required.

SUMMARY

1. A case of traumatic necrosis of the subcutaneous fat of the new-born infant is presented, with clinical and histologic observations.

2. The symptomatology, pathology and etiology of the condition are reviewed.

321 Metz Building, Grand Rapids, Mich.

28. Longcope, W. T.: Hypoglycemia in Scleroderma, J. A. M. A. **90**:1 (Jan. 7) 1928.

BILATERAL GANGRENE OF THE FEET FOLLOWING TONSILLECTOMY *

IRVING SHERWOOD WRIGHT, M.D.
NEW YORK

A search of the literature has failed to reveal a single instance which parallels the case herein reported. Three features, each a most unusual sequel of tonsillectomy, are outstanding: (*a*) a markedly septic course with development of a heart murmur, (*b*) bloody stools and (*c*) gangrenous areas on both feet, involving the toes, followed by clinical recovery except for a residual systolic cardiac murmur and the loss of one toe.

REPORT OF CASE

History.—J. R., a girl, aged 2 years, 3 months, of Italian parentage, was admitted to the hospital for tonsillectomy and adenoidectomy on March 3, 1928. At that time the heart was of normal size and shape and murmurs were not heard; except for hypertrophied tonsils and adenoids the results of the physical examination were negative. The past history of the child was that of a normal, healthy child without previous illnesses, except for repeated attacks of tonsillitis. The stools had always been normal in color, consistency, form and number, and blood had never been observed to be present.

The family history was negative, except for one miscarriage.

Tonsillectomy and adenoidectomy were performed on March 3, without hemorrhage or immediate difficulty. The following day the patient was discharged in good condition; there was no fever or hemorrhage and the fossae presented the average appearance of tonsillar fossae one day after operation.

On March 5, the day following discharge from the hospital, the child became feverish. The temperature rose to 101 F. that afternoon. From March 5 until March 13, the temperature ran a septic course. On March 9, and for the next four successive days until March 13, the patient had large amounts of bright red blood in every stool. There were three or four stools each day. After treatment with a chalk mixture and starvation, the bleeding from the intestines ceased. The temperature dropped to normal and remained thus until March 18 (five days) when the patient developed a high fever with general malaise and anorexia, which were constant until admission.

Physical Examination.—The feet were apparently normal on March 19, 1928. On March 20, the morning of the second admission, the mother noted that the third toe on the right foot was black and the fourth toe on the left foot was dull red. A spot over the left external malleolus later became a dull purplish color. These affected parts all became progressively darker in color during the twelve hours preceding admission.

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* From the Department of Pediatrics, New York Post-Graduate Medical School and Hospital.

Physical examination on the second admission to the hospital revealed the following positive observations:

The patient was a well nourished and well developed girl apparently acutely ill. The tonsillar fossae showed that the enucleation had been complete. The right fossa was clean and healed. The left fossa still contained a grayish slough. The heart rate was rapid (135, p. m.). The sounds were pounding, and the first sound was definitely roughened. The area of cardiac dulness was not enlarged. The lungs were normal as to resonance, voice and breath sounds and râles were not heard. The liver was of normal size, and the spleen was barely palpable. Palpation did not reveal any abnormal masses in the abdomen.

Pathologic changes were not apparent in the upper extremities, genitalia and reflexes.

Examination of Lower Extremities.—The third toe on the right foot showed a definite gangrenous process which involved the entire toe. There were also several small gangrenous areas on the side and inner border of the foot varying from 1 to 2.5 cm. in diameter.

Fig. 1.—Some of the gangrenous areas on each foot including involvement of the toes. Note that the fourth toe on the right foot and the third and fourth toes on the left foot show marked swelling although the changes in color are not noticeable in the photograph.

The fourth toe on the left foot was purple; apparently a beginning gangrenous process was in progress. There was also a gangrenous area about 2 cm. in diameter over the external malleolus. The pulsations of the dorsali pedi arteries were palpable in both feet. The gangrene was dry in type with small blebs over the gangrenous areas.

Course and Treatment.—Two days after admission (March 22), a soft but easily audible systolic murmur was heard over the mitral area, which was not transmitted elsewhere. The blebs over the gangrenous areas increased in size. They were incised, and a culture of the contained fluids taken which proved to be positive for *Streptococcus hemolyticus*. The course of the condition was progressively worse until March 28. Examination on March 27, showed a terminal gangrene of the second, third and fourth toes of the right foot, and the fourth toe of the left foot, with a moderate cellulitis of both legs and ankles.

The temperature curve was septic varying between 100 and 105 F. for the first eight days after admission, after which it never rose above 100 F. The pulse rate was 130 per minute on admission, but dropped to normal in accordance with the fall in temperature. Respiration varied between 26 and 18 per minute.

The treatment consisted of applications of dry heat under a cradle and dry dressings. Fluids were forced.

The gangrenous spots slowly cleared up, turning from purple to red and then fading to normal, except for the end of the third toe of the right foot which became dry and partly fell off. A small additional section was clipped off, thus losing the two distal phalanges; following this the small stump healed completely.

The patient never complained of exquisite tenderness, though she did cry at night, so mild sedatives were given at first.

Laboratory Observations.—A blood count on admission showed: red blood cells, 4,197,000; hemoglobin, 70 per cent; white blood cells, 10,000; polymorphonuclears, 88 per cent; small lymphocytes, 3 per cent; large lymphocytes, 9 per cent.

Fig. 2.—Fading of gangrenous areas and the healed stump of the third toe of the right foot which sloughed off.

Chemical examination of the blood showed: uric acid, 4.3 mg. per hundred cubic centimeters; sugar, 0.116 mg. per hundred cubic centimeters; carbon dioxide, 56 per cent; calcium, 10.7.

Repeated cultures of the blood failed to isolate any organism from the blood stream.

The Wassermann reaction of the blood, repeated examinations of the urine and vaginal smears were negative.

Condition at Time of Discharge.—The condition of the patient progressively improved, both locally and generally after March 28. After six weeks the areas of gangrene had practically cleared up, being replaced by normal skin. The stump of the third toe of the right foot was completely healed.

The heart murmur was still audible as a soft systolic murmur over the apex. It was not more marked.

The patient was discharged on May 1, 1928, apparently in excellent health, without pain or fever. She was able to play about the ward for several days before discharge.

Six weeks later, the child was apparently in excellent health and leading a normal life.

COMMENT

Three possible explanations of the mechanism of this symptom complex present themselves for consideration.

1. The tonsillectomy was not the exciting factor, but the time relationship between the tonsillectomy and the appearance of the gangrene was only one of coincidence. This seems untenable, since the symptoms began with more mild manifestations on the second day after operation and became progressively worse, finally reaching the height of severity with the appearance of the gangrene. There were no signs or symptoms before the operation premonitory of the symptom complex following, and no other possible exciting cause was ever found. Therefore, I was forced to conclude that the tonsillectomy and adenoidectomy were the exciting factors in this instance.

2. The second possible mechanism to be considered was that the tonsillar fossae themselves gave rise to showers of bacterial emboli which were distributed to the endarterioles of the affected areas; namely, the endarterioles of the mesenteric vessels giving rise secondarily to bloody stools and to the endarterioles supplying the areas of the feet which became gangrenous. The fact that the slough remained in the left tonsillar fossa until the twenty-second day after operation would tend to strengthen this explanation.

It is difficult, however, to trace a path through the blood stream by which emboli could travel from the tonsillar fossae to the mesenteric vessels and feet without being caught in the lungs or liver.

Koplik [1] described a case of septicemia following tonsillectomy which presents a few of the features found in the case under consideration. The patient in this case developed a septic temperature, bled from the bowels, and showed numerous ecchymotic areas under the skin. There was also a severe progressive anemia, and a systolic cardiac murmur at the apex, which evidently was hemic since it disappeared following a transfusion. The patient recovered completely, showing no residue. While Koplik's case presents some of the features found in our patient the mechanism was evidently different in nature. Koplik described it as, "True hematogenous sepsis following tonsillectomy and adenoidectomy."

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1. Koplik, Henry: Infections Following Tonsillectomy with a Consideration of the Forms of Such Infections, Am. J. M. Sc. **144**:30, 1912.

3. The third possible explanation of the mechanism causing this symptom complex involves the heart valves as secondary foci of infection from which bacterial emboli were distributed. Moore [2] mentioned a case of "acute ulcerative endocarditis which resulted from amygdalectomy." In the present case, a systolic cardiac murmur developed, which was heard the best over the mitral area following the tonsillectomy. This was associated with and followed by bleeding from the bowels and the development of the gangrenous areas on the feet. It seems possible therefore that the tonsillectomy was an exciting factor to the development of an acute vegetative endocarditis, and that bacterial emboli were thrown off into the circulation reaching the endarterioles of the mesenteric vessels and the affected areas of the feet. The structure of the circulatory system would allow the emboli to travel to these endarterioles without passing through any finer network of vessels such as presented by the lungs and liver.

There were apparently three sets of embolic showers: (*a*) to the mesenteric vessels, on the third or fourth day after operation, (*b*) to the vessels of the feet on the fourteenth day after operation and (*c*) again to the vessels of the feet on the twenty-second or twenty-third day after operation. Further embolic showers did not occur.

The apparent clinical recovery of this patient is not the least unusual feature of this case.

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2. Moore, S. E.: The Dangers and Complications of Tonsillectomy, M. J. & Rec. **90**:972 (Dec. 2) 1916.

PURPURIC EXANTHEMS IN INFECTIOUS DISEASES *

H. BAAR, M.D.
VIENNA, AUSTRIA
AND
B. M. GASUL, M.D.
CHICAGO

In spite of the manifold clinical manifestations of purpura, the older investigators considered all forms of this symptom-complex as manifestations of the same disorder. Later the investigations of Hayem,[1] Bensaude and Rivet [2] and Duke [3] concerning the changes in the blood platelets, bleeding time and retraction of the blood clot resulted in the separation of the chronic purpura hemorrhagica, the morbus maculosus werlhofii, from the other forms of purpura. In the German literature, however, the unitarian views of all the purpuras held by Scheby-Buch [4] and Litten [5] were still the outstanding ones until the work of Frank [6] of Breslau, who proved the special place occupied by Werlhoff's disease. Even now, however, the fact that purpura is only a symptom, and that it may be due to various etiologic factors, such as disturbances of the blood-forming organs, diseases of the walls of the blood vessels, endocrine, and even nervous disturbances (Lehndorff [7]) is still not generally recognized, and attempts have been made to divide all purpuras according to the presence or absence of thrombopenia. Schultz,[8] for example, recognizes a thrombopenic and an athrombopenic purpura. In the pediatric literature, Glanzmann [9] recognizes the morbus maculosus

* Received for publication, July 19, 1928.

* From the St. Anna Children's Hospital, Vienna, Austria. Romeo Monti, M.D., Director.

1. Hayem, G.: Compt. rend. Soc. de biol. **53**:45, 1901.

2. Bensaude, P., and Rivet, L.: Arch. gen. de méd. **1**:193, 1905.

3. Duke, W. W.: The Pathogenesis of Purpura Hemorrhagica with Especial Reference to the Part Played by Blood Platelets, Arch. Int. Med. **10**:445 (Nov.) 1912.

4. Scheby-Buch: Deutsches Arch. f. klin. Med. **14**:466, 1874.

5. Litten, M.: Die hemorrhagischen Diathesen, in Nothnagel: Spezielle Pathologie und Therapie, Vienna, Alfred Hölder, 1908.

6. Frank, E.: Berl. klin. Wchnschr. **18**:454, 1915; **19**:490, 1915.

7. Lehndorff, H.: Zur pathogenese und Systematik der purpura erkrankungen, Berlin, Julius Springer, 1925.

8. Schultz, W.: Ergebn. d. inn. Med. u. Kinderh. **16**:32, 1919.

9. Glanzmann, E.: Jahrb. f. Kinderh. **83**:271, 379, 419, 1916; **88**:1, 113, 1919; **91**:391, 1920.

werlhofii (in the sense of a hereditary hemorrhagic thrombopenia) and an anaphylactoid purpura. Pfaundler and Sebt [10] soon showed the weakness of this classification, and it is due to their work that the characteristic, well defined, clinical picture of Schönlein-Henoch's purpura has now been separated from the diverse hemorrhagic diathesis of the various infectious diseases. But even the classification of Pfaundler and Sebt, who differentiate three main groups of purpuras—the Schönlein-Henoch's purpuras, the purpuras of the acute and chronic infectious diseases and the purpuras of the diseases of the blood-forming organs—has been shown by Baar [11] to be inadequate. This classification includes under one group diseases which are pathogenically heterogenous. In the same group with the classic chronic purpura hemorrhagica are the leukemias, the anemias and the diseases of the liver. Baar, therefore, came to the conclusion that an adequate classification of all purpuras is not possible, and that purpura should be looked on only as a symptom. This symptom, however, may at times be the outstanding manifestation of a clinically and even hematologically well defined disease. As such we consider Schönlein-Henoch's purpura and the morbus maculous werlhofii. The purpuras that are seen in the various infectious diseases, in poisonings, in metabolic disorders and in nutritional disturbances are entirely different, and are caused by different factors. In cases of epidemic cerebrospinal meningitis and pyocyanic sepsis, they are due to mycotic embolic phenomena (Benda,[12] Pick,[13] Bourdelli,[14] Battley;[15] in cases of septic endocarditis, the purpuric spots are due to certain changes in the walls of the blood vessels (Chiari and Baar [16]). Pathogenically, they may even show certain resemblances to Werlhof's disease, as in diphtheria (Duke [17]) or in typhus (Herz,[18] Kaznelson [19]), and finally they may have common characteristics with Werlhof's or Schönlein and Henoch's purpura and still differ from them classically. It is this last form that is of great interest, because it is often confused with Werlhof's disease.

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10. Pfaundler, M., and Sebt, L.: Ztschr. f. Kinderh. **19**:235, 1919.
11. Baar, H.: Die Blutungsübel, in Baar and Stransky: Die klinische Hämatologie des Kindesalters, Vienna, Franz Deuticke, 1928.
12. Benda, C.: Berl. klin. Wchnschr. **17**:449, 1916.
13. Pick, L.: München. med. Wchnschr. **52**:2869, 1912.
14. Bourdelli, L. B.: Centralbl. f. Kinderh. **18**:773, 1925.
15. Battley, S.: Purpura Fulminans Due to Meningococcus, Am. J. Dis. Child. **33**:244 (Feb.) 1927.
16. Chiari, H., and Baar, H.: Wien. klin. Wchnschr. **39**:1123, 1926.
17. Duke, W. W.: Causes of Variation in the Platelet Count, Arch. Int. Med. **11**:100 (Jan.) 1913.
18. Herz, A.: Wien. klin. Wchnschr. **22**:675, 682, 1917.
19. Kaznelson, P.: Deutsche Arch. f. klin. Med. **128**:131, 1919.

In this article, three such cases are reported. The purpura in the first case appeared during the course of scarlet fever. The purpura in the second case was seen in a patient who had an infection of an unknown etiology, this case being of interest also on account of the unusual localization of the purpuric exanthem. The third case is that of a hemorrhagic diathesis in septic diphtheria, which showed the clinical, hematologic and pathologic symptoms of a true Werlhof's disease.

REPORT OF CASES

CASE 1.—*History.*—G. M., a girl, aged 7, became suddenly ill on Nov. 16, 1927, with fever, vomiting, sore throat and an exanthem. She had had measles and chickenpox about one year previously; otherwise her past history was unimportant. She entered the St. Anna Children's Hospital of Vienna on Nov. 16, 1927, with a condition diagnosed as scarlet fever.

Examination.—The outstanding observations at the time of admission were: a typical scarlet red, uniform eruption covering the whole body, with the central portion of the face showing the characteristic circumoral pallor. The Rumpel-Leede test was positive; the temperature was 104.7 F.; the submaxillary glands were enlarged and painful to pressure; a typical strawberry tongue was present; the pharynx and tonsils were inflamed and reddened. A splenic tumor, however, was not found. Other pathologic conditions were not present. The Pirquet reaction was negative. The temperature dropped to normal four days later. On the fifteenth day of the disease, the temperature again rose to 100.7 F., and a pale, morbilliform eruption appeared on the face, body and extremities. On the next day, the cervical glands became swollen, and the exanthem was more scarlatiniform. On the next day, numerous small petechiae appeared on the extensor surfaces of both upper and lower extremities. The blood count was as follows: hemoglobin (Sahli's method), 65 per cent; red blood cells, 4,400,000; white blood cells, 16,200; blood platelets, 25,000 per cubic millimeter. (The blood platelets were counted twice by the Fonio and by Baar's methods. Baar's method is a combination of Langmeyer's and Kristensen's methods.) The differential count showed: single segmented leukocytes, 1 per cent; polymorphonuclear neutrophils, 63 per cent; lymphocytes, 21 per cent; monocytes, 6 per cent; no eosinophils and no basophilic granulated leukocytes. The fragility test (Simmel's method) was normal; bleeding time (Duke's method) was four minutes; the coagulation test showed reaction time two minutes, and coagulation time thirteen minutes (Sahli-Fanio's method). There was incomplete retraction of the blood clot. The blood platelet count on December 6 was 125,000; on December 7, 185,000, and on December 12, 210,000. The bleeding time on December 7 was two minutes. The petechiae disappeared within five days and have not recurred. The child was discharged from the hospital on Dec. 28, 1927.

Summary.—A girl, aged 7, entered the hospital with a typical case of scarlet fever; fifteen days later, at the time when the second eruption occasionally appears, a cervical lymphadenitis and a morbilliform scarlatiniform erythema reappeared and was followed by numerous definite petechiae on the extensor surfaces of the extremities. A high grade thrombopenia of short duration with a disturbance of the retraction of the blood clot was noted; the bleeding time was normal. The condition reminded one of Schönlein-Henoch's purpura, so far as the localization of the purpura and the erythema were concerned. The other man-

ifestations of the Schönlein-Henoch's purpura, however, were lacking, and the blood platelet count was also too low. On the other hand, as compared to Werlhof's disease, the bleeding time was normal, contrary to the constant observation of prolonged bleeding time in Werlhof's disease, and the clinical manifestation was, of course, also different from that noted in Werlhof's disease. The bleeding time, however, does not always run parallel to the platelet count (Roskam,[20] Magnus [21]). The fibrinogen content and the contractions of the capillaries, as well as their ability to absorb the colloids necessary to stabilize the platelet suspension, must also be considered. In this case of purpura, it must be remembered that the petechiae appeared about the time the second eruption usually appears. At this time, the erythematous eruption is occasionally seen, but in this case the probable injury to the vessel walls was so great that a high grade thrombopenia resulted. Thrombopenia is occasionally seen in cases of scarlet fever as well as in other infectious diseases without purpuric manifestations (Tchistowitsch [22]).

CASE 2.—*History.*—J. W., a girl, aged 5½, entered the St. Anna Children's Hospital on Nov. 24, 1927, with the following history: five days previous to the time of admission, the child became suddenly ill with high fever and pains in the mandibular regions. Red patches appeared first on the right cheek and then on the left, extending over the regions of the ear.

Examination.—The examination on entrance revealed numerous dark red, nonconfluent maculopapules over both parotid regions, extending downward on the neck; these did not disappear on pressure. This hemorrhagic exantham was symmetrical, but more marked on the left side of the face. A few scattered hemorhagic maculopapules could also be seen in the region of the left shoulder. The skin of the inner surfaces of both thighs was also covered with numerous light red macules, which, however, disappeared on pressure. The Rumpel-Leede test was negative; the teeth were carious; many fine râles were heard over the lower lobes of both lungs, but other pathologic conditions were not present. The eruption began to disappear on the fourth day. The eruption on the thighs became hemorrhagic on the second day. Two days later, the entire purpura began to fade. The photographs were taken at this time (figs. 1 and 2). Observations on the blood at the time of entrance were: red blood cells, 4,750,000; white blood cells, 15,700; hemoglobin (Sahli's method), 75 per cent; blood platelets, 190,000. The differential count showed: eosinophils, 0; basophils, 0; single segmented neutrophilic leukocytes, 5.5 per cent; polymorphonuclear neutrophilic leukocytes, 63 per cent; monocytes, 3 per cent; lymphocytes, 28.5 per cent. The bleeding time (Duke) was one and a quarter minutes; the reaction time was three minutes. Complete coagulation occurred in sixteen minutes (Sahli-Fanio's method). There was normal retraction of the blood clot. The fragility test (Simmel's method) was normal (5,000,000 red blood cells with physiologic sodium chloride; 4,800,000 with 0.7 per cent; 3,800,000 with 0.6 per cent; 2,280,000 with 0.5 per cent; 2,800,000 with 0.4 per cent and 0 with 0.3 per cent). On November 28 the white blood cells numbered 12,000, the blood platelets, 300,000. On November 29 the white blood cells numbered 9,500; the blood platelets, 280,000; the differential count showed metamyelocytes, 1 per cent; segmented neutrophils, 54 per cent; lymphocytes, 42 per cent, and eosinophils, 2 per cent.

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20. Roskam, J.: Compt. rend. Soc. de biol. **85**:18, 733, 1921; Presse méd. **31**: 472, 1923.

21. Magnus, G.: Arch. f. klin. Chir. **130**:237, 1924.

22. Tchistowitsch: Folia haematol. **4**:295, 1907.

Comment.—In this case, at the end of an acute infection a symmetric purpura appeared in the parotid region and an erythema on the surfaces of the thighs. This erythema became hemorrhagic a few days later. The observations on the blood were neutrophilic leukocytosis with a change to the left and eosinophilia, normal blood platelet count, normal bleeding, coagulation and retraction time. The pains in the mandible, the symmetrical appearance of the purpura and the combination with the erythema may make one think of Schönlein-Henoch's purpura. Still, the course of the disease, the unusual localization of the eruption and especially the high fever at the beginning of the disease, as well as the morphologic

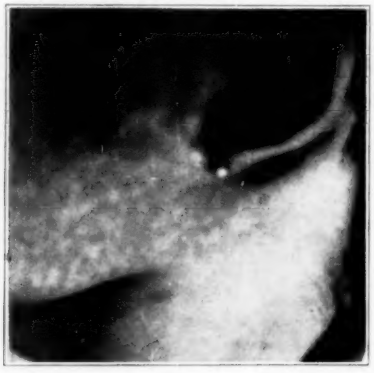

Fig. 1 (case 2).—Unusual localization of the purpuric eruption.

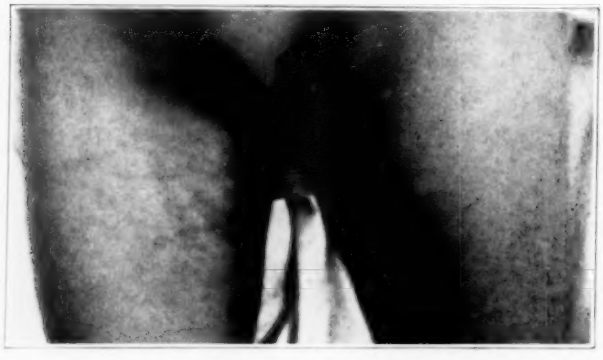

Fig. 2 (case 2).—Symmetrical localization of the purpura.

blood picture, speak against it. We are in full agreement with Pfaundler and Sebt's statement to the effect that in cases of Schönlein-Henoch's purpura, the patients show either no fever or a slight rise in temperature. In our case, the morphologic blood picture showed leukocytosis and an increase in the polymorphonuclear neutrophils with the appearance of single segmented leukocytes and metamyelocytes and eosinophilia. This observation on the blood, together with the fever, speaks for an infectious etiologic agent (the neutrophilic phase in the sense of Schilling). The cases described by Lenoble [23] under the name "erythemes infec-

23. Lenoble, E.: Ann. de dermat. et syph. **3**:1097, 1902.

tieuse hemorrhagiques a forme purpurique" are similar to our case, although we do not subscribe to Lenoble's classification of purpuras on a purely hematologic basis. We cannot explain the unusual localization of the purpura. The capillary function test on the arm was negative in our case, and we must assume a disturbance of the capillaries only in a definite symmetrical section. French authors consider an injury to the spinal tract probable in the cases of symmetrically located purpuras (purpura myelopatique after Faison). Castex [24] found definite histologic changes in the tractus intermedius lateralis of the spine in two cases of symmetrical purpura. Morowitz [25] said that he believed there was a probability of central involvement of the vessel.

CASE 3.—*History.*—L. J., a girl, aged 4, entered the hospital on Sept. 15, 1927, with the following history: The illness began five days prior to the time of admission, with fever and a sore throat; during the last day, swelling in the neck, irritability and difficulty in speech occurred; otherwise the history was insignificant.

Examination.—The child was restless; the color of the skin was pale, and the lips were slightly cyanotic. The temperature ranged from 101 to 100.7 F.; there was a strong offensive odor; the tongue was heavily coated, the tonsils meeting in the midline; the uvula was greatly edematous, and a high grade inspiratory dyspnea with retraction of the epigastric and intercostal spaces was present. Both tonsils were covered with a dirty-grayish membrane. The peritonsillar tissues were markedly infiltrated, without fluctuation. The lungs were normal to percussion, but diffuse râles were present over both lungs. The borders of the heart were within normal limits; the heart tones were clear; the pulse rate was 150; the pulse was faint and hardly perceptible. Neither the liver nor the spleen was enlarged. Laboratory examination revealed many diphtheria bacilli in the throat. The child was given 18,000 units of diphtheria antitoxin intramuscularly. On September 17, she had a severe nosebleed, which recurred on September 19. On this day, numerous ecchymoses appeared over the entire trunk. The relative tract dulness was now 1 cm. to the right of the right border of the sternum and on the left 1.5 cm. to the left of the midclavicular line. The liver was two fingerbreadths below the costal margin. On September 20, the liver was three fingerbreadths below the costal margin and was painful to touch. There was gallop rhythm, more ecchymoses and more nosebleed. Epinephrine and physiologic sodium chloride solution were given subcutaneously several times daily. On September 21 the patient died.

Observations on the blood on September 19 were as follows: hemoglobin (Sahli's method), 60 per cent; red blood cells, 4,120,000; white blood cells, 16,700; blood platelets, 21,300. The differential count showed: basophils, 0; eosinophils, 0; metamyelocytes, 1.5 per cent; single segmented leukocytes, 8 per cent; polymorphonuclear neutrophils, 61.5 per cent; monocytes, 2.5 per cent; lymphocytes, 26.5 per cent. Moderate polychromatophilia and anisocytosis were present, but nucleated red blood cells were not found. The bleeding time was fifteen minutes; reaction time, three minutes; coagulation time, seven minutes (Sahli-Fanio's method). Retraction of the blood clot did not occur after twenty-four hours. On September 20, the blood platelets numbered 13,500 per cubic millimeter.

The pathologic observations (assistant, Dr. Musger) were as follows: The tonsils were greatly enlarged, the soft palate, especially the uvula, was edematous.

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24. Castex, M. R.: Presse méd. **32**:277, 1924.

25. Morowitz, P.: Med. Klin. **16**:769, 1923; München. med. Wchnschr. **38**: 1558, 1926.

The tonsils and the uvula were covered with a dark grayish, closely adherent membrane. The epiglottis was slightly reddened. Changes were not present in the larynx. Small punctiform hemorrhages were present over the apex of the left lung; a few scattered areas showing evidence of bronchopneumonia were noted in the lower lobe of the right lung; the liver and kidneys appeared pale; the splenic pulp was somewhat more prominent; the size of the heart was increased in length and width; the myocardium was pale; the papillary muscles and trabeculae were greatly flattened; thrombi were present in the right auricle; small hemorrhages were seen when the interventricular septum was sectioned; changes were not present in the valves. Smears and sections of the bones were made and stained with May-Grünwald and Pappenheim stains. For comparison, we used stains and sections of bones from patients of the same age who had tuberculous meningitis and pneumonia. A slightly larger number of megalokaryocytes were seen. Their nuclei were compact, stained a dark brown and were pyknotic, but Schridde's azure granules were not seen in the plasma of the megalokaryocytes. Only a few granules were seen in some; these were closely packed in one part of the protoplasm and did not appear to be normal.

Comment.—In this case, a blood picture is presented that is morphologically and pathologically similar to that found in true Werlhof's disease. In Werlhof's disease, the megalokaryocytes are little affected (Lantier, Oberling and Woringer,[26] Engel,[27] Foerster,[28] Sternberg,[29] Frank,[30] Kaznelson [19]). These same authors, however, showed absence of azure granules, disorderly granulations, pyknosis and karyorrhexis as in Werlhof's disease. In estimating the nuclear pyknoses of the megalokaryocytes, one must remember the fact that pyknosis often takes place after death (Askanazy [31]). But the differences in the bones of the patient with diphtheria and those of our patient were so marked that we do not hesitate to state that marked pyknosis was present. Duke produced experimentally the blood picture of Werlhof's disease by injecting animals with diphtheria toxin.

CONCLUSIONS

The various manifestations of purpura in infectious diseases make an adequate classification of this symptom-complex impossible. Our cases show striking similarities to Werlhof's disease and to Schönlein-Henoch's purpura, but careful investigations show the condition to be entirely different. A case is presented in which a purpuric exanthem appeared at the time of the second eruption in scarlet fever. The localization of the lesion was similar to that in Schönlein-Henoch's purpura,

26. Lantier, H.; Oberling, and Woringer: Rev. franç. de pédiat. **3**:340, 1927.

27. Engel, E.: Arch. f. klin. Chir. **129**:563, 1924.

28. Foerster, A.: Ztschr. f. klin. Med. **92**:170, 1921.

29. Stern and Hartmann, E.: Ztschr. f. klin. Med. **104**:490, 1926.

30. Frank, E.: Die hemorrhagischen Diathesen, in Schittenhelm: Krankheiten des Blutes und der Blutbildenden Organe, Berlin, Julius Springer, 1925.

31. Askanazy, M.: Knochenmark, in Henke, Lubarsch: Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, Julius Springer, 1927, vol. 1 and 2.

but the blood platelet count was too low. This case shows also that the bleeding time is not always parallel to the number of blood platelets present.

Another case of purpura due to some unknown infection with a peculiar localization of the eruption is also described. Finally, we presented a case of a hemorrhagic diathesis in the course of a septic diphtheria, which showed the clinical, hematologic and histologic characteristics of true morbus maculosus werlhofii.

ADENOCARCINOMATOSIS IN A GIRL AGED SIX YEARS*

GEORGE M. LYON, M.D.

J. S. KLUMPP, M.D.
HUNTINGTON, W. VA.

AND

J. W. FERGUSON, M.D.
KENOVA, W. VA.

We feel justified in reporting this case because of the rarity of the condition in patients of this age. The case brings out the value of the intradermal tuberculin test (0.1 or 1 mg.) in differentiating between a tuberculous and a nontuberculous condition. The presence of mitotic figures in the cells of the punctate was suggestive of a malignant condition rather than of a tuberculous process.

A review of the literature has not been attempted in this report.

REPORT OF CASE

History.—L. B., a white girl, aged 6 years, was first seen in consultation on May 6, 1925. Her chief complaint was an enlarged abdomen and increasing weakness. There had not been a similar condition in the family, nor had there been any tuberculosis or cancer.

The patient had been a child somewhat below average health and sturdiness until the present illness had begun. She had had measles at 3 years of age and an unexplained exanthem at 5 years of age. Her diet tended to the starchy type of food with little protein. She was never strong enough to play vigorously with other children. For several weeks previous to the first recognized signs of sickness, she had seemed less active than usual, and for about ten days before the examination on May 6, her mother had noticed that she could not sit and hold her baby sister on her lap as was her custom. The mother had noticed on further examination that the child's abdomen was greatly swollen, so much so that it prevented her from sitting and holding the baby. On May 2, the patient had been taken to the Rife-Ferguson Hospital. At this time she had fluid in the abdomen, but there was no fever. On May 4, she had a temperature of 101 F. and the abdomen was essentially as it had been two days previously. Two days later (May 6) she was seen in consultation, and the following observations were made.

Her appetite had been poor for several weeks, and since April 25 she had been voiding infrequently. She had not coughed. Her color, usually pale and not good, had been worse the ten days previous to the consultation. The stools had contained bile pigments, but were otherwise not remarkable. There had been neither hemoptysis nor hematemesis. There had been profuse night sweats for many weeks with a loss of weight. A slight fever had been present at times, but as a rule there was none.

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On May 6, the temperature was 100 F., the pulse, 90 and the respiration, 24. The patient was a thin, emaciated white girl of about 5 years of age, with a yellowish pallor and a tensely distended abdomen. She was lying on her back and had moderate dyspnea; there was a short grunting type of respiration. There was neither petechiae nor icterus. The lymph glands were not enlarged generally or locally. The head, eyes, ears, nose, mouth, pharynx, tonsils, neck, thyroid and spine did not show any remarkable characteristics. The chest was distended in the lower third, and there was a large costal angle of about 150 degrees. Measured at the lower costal margin, the chest was 22 inches (55.52 cm.) in circumference. The lungs were normal to percussion and auscultation. The heart was somewhat elevated above its normal position. The point of maximum impulse and the apex thrust were to the left of the normal position. The heart appeared to have been in a position more transverse than normal, and did not seem to be enlarged. There were no shocks or thrills. The heart sounds were regular in rate and rhythm, but the first sound at the apex and the character of the pulse gave one the impression of a myocardium that was not normally vigorous. The pulse rate was 90 and regular as was the rhythm, but the pulse was of small volume. The blood pressure in the arms was 100 systolic and 60 diastolic, and in the legs, 105 systolic and 65 diastolic. The abdomen was distended, measured midway between the xiphoid and the umbilicus, the circumference was 26½ inches (67.23 cm.). Measured at the umbilicus it was 28 inches (71.12 cm.). Measured midway between the umbilicus and the symphysis pubis, it was 22 inches (55.52 cm.). There was a definite fluid wave on percussion and palpation. Masses were felt only in the left upper quadrant; on deep palpation there was a resistance suggesting a soft, enlarged mass which did not feel like an enlarged spleen. There was moderate tenderness in this region and there had been moderate pain at times during the week previous to this examination. The liver, spleen and bladder were not palpable. The genitalia, rectum, legs, joints and skeletal and neurologic observations were not remarkable. There was no edema of the dependent parts, ankles or conjunctivae.

Laboratory Examination.—The examination of the blood on May 6, showed: red blood cells, 3,000,000; white blood cells, 12,000, and hemoglobin (Sahli) 55 per cent. The differential white cell count was: polymorphonuclear neutrophils, 81 per cent; polymorphonuclear eosinophils, 0; polymorphonuclear basophils, 0; small mononuclears, 14 per cent, and large mononuclears, 5 per cent.

The red blood cells contained a good amount of hemoglobin. There was neither anisocytosis nor poikilocytosis. There were no unusual leukocyte forms or parasites. There was almost a complete absence of platelets. The intradermal tuberculin test (0.1 mg.) gave negative results.

On May 8, the results of the urinalysis showed the voided specimen to be cloudy, yellow, acid, with a specific gravity of 1.010; the urine was negative for albumin and sugar, and the results of the microscopic examination were negative. The intradermal tuberculin test (1.0 mg.) was negative. The physical condition was unchanged, except that the patient was weaker and suffering more with abdominal distention.

On May 10, the phenolsulphonphthalein test for renal function gave a return of 40 per cent of the dye in one hour and 20 per cent more the second hour.

The abdomen had increased in size until it was 29 inches (73.66 cm.) in circumference at the umbilicus and 23 inches (58.42 cm.) midway between the umbilicus and the symphysis pubis.

Paracentesis abdominalis was performed 4 inches (10.16 cm.) below the umbilicus in the midline, and 5 liters of a serosanguineous fluid was removed.

There was a slightly unpleasant odor to the fluid. After the fluid was removed, the measurement at the lower margin of the chest was 20 inches (50.80 cm.); at the upper part of the abdomen, 21 inches (53.34 cm.); at the umbilicus 19 inches (48.26 cm.), and at the lower part of the abdomen, 19 inches.

The punctate on examination showed a specific gravity of 1.022. It gave an alkaline reaction to litmus. It was of a bloody, straw color, and on shaking yielded a persistent foam that was white and not greenish. There was a heavy cloud of coagulation on the application of heat and acetic acid. Reducing bodies were not present. A microscopic examination of the centrifugalized specimen showed some red blood cells and a few ordinary leukocytes, but a great many cells which were much larger than leukocytes. The protoplasm stained well with eosin and the nuclei well with hematoxylin. With this stain or with Wright's stain, the nuclei of approximately half of these cells showed mitotic figures. The cells were extremely fragile. They closely resembled the cells seen in the punctates from carcinomatosis of serous surfaces seen in adults. There were few eosinophil leukocytes. There were no parasites, tubercle or other bacilli. Bacteriologic cultures were sterile. A guinea-pig inoculated intraperitoneally with some of the punctate remained well, and a subsequent autopsy did not reveal evidences of tuberculosis or other bacterial infection.

At this time an exploratory laparotomy was recommended, and the family was advised that there was a malignant process present rather than a tuberculous peritonitis. Operation was refused temporarily.

On May 12, the fluid had recurred rapidly, and the abdomen measured 21 inches at the costal margin, 23 inches in the upper half, 22½ inches (56.77 cm.) at the umbilicus and 20 inches at the lower half. The results of the urinalysis were again negative.

By May 15, the weakness had steadily progressed and the general health had failed. The abdominal measurements, taken as before, were 21½ (54.61 cm.) 25½ (64.73 cm.), 23½ (59.69 cm.) and 22 inches, respectively.

On May 17, the abdominal measurements were 22, 26½, 28 and 22 inches, respectively. A second paracentesis abdominalis was performed and 6 liters of fluid removed. The fluid was similar to that removed previously.

On May 22, after a steadily progressive increase in the weakness, the parents consented to the operation, and on this date Dr. Klumpp and Dr. Ferguson performed an exploratory laparotomy. Their notes were as follows: A lower right rectus incision was made. There was a considerable gushing of serosanguinous fluid when the peritoneum was incised. As much fluid as possible was removed. The intestinal loops were moderately distended and were a scarlet red, with considerable injection of the superficial vessels. The cecum was delivered with ease after the friable exudative adhesions to the contiguous bowel had been removed. Entirely surrounding the cecum, ileocecal junction and proximal portion of the ileum, were numerous reddish, frondlike clusters. There were smaller clusters of the same material clinging to the small intestine, distal to the cecum. The appendix appeared as a pallid stalk projecting from the vegetative growth. The appendix with its warty excrescences was removed for pathologic examination. The stump was ligated and inverted with a purse-string suture. The peritoneal cavity and the wound were closed without drainage. No attempt was made to explore the left side of the upper part of the abdomen. The postoperative course was entirely uneventful except that the fluid began to refill the abdomen and by the fourth day after the operation there were again unmistakable signs of free fluid in the abdomen. The patient was discharged from the hospital on May 28, six days after the operation. The wound was clean, having healed per primam.

On May 25, the pathologic examination of the appendix and adnexa was made by Dr. F. C. Hodges, who gave the following report: The appendix was small and hard with outgrowths of warty excrescences along the mesenteric border, varying in height from 3 to 7 mm. The microscopic sections showed a lymphoid hyperplasia in the appendix. The excrescences were adenocarcinoma of mixed columnar and cuboidal cells.

From May 28 until her death on August 9, nothing of special interest was observed. The patient grew weaker, and the emaciation increased steadily until she died with general asthenia. Evidences of metastases to other parts of the body were not found. Pigmentations of the skin were not present. The patient did not have fever at any time after the operation. The fluid recurred rapidly, so rapidly in fact that it was necessary to perform an abdominal paracentesis every second day from the time she left the hospital until two weeks before her death. The character of the fluid did not change. During the last two weeks of life, the abdomen was tapped only three times. Masses were not palpable in the abdomen at the time of death. Autopsy was refused.

ANEMIA OF THE NEW-BORN INFANT*

EVELINA W. EHRMANN, M.D.
CHICAGO

The following case of anemia in a new-born infant is the sixth to be reported.[1] All six cases are characterized by pallor, moderate or severe, noticed within the first twelve days of life. The number of red cells varied from 2,500,000 to 980,000; the hemoglobin content from 48 per cent to 20 per cent; the hemoglobin index from 0.64 to 1.3, and the number of white cells from 10,600 to 68,400. The morphology of the white cells was normal except for an occasional myelocyte. The ratio of lymphocytes to leukocytes was normal, reduced or increased. Myelocytes, though few in number, were seen in most cases. The red cells generally showed achromia, polychromatophilia, anisocytosis and poikilocytosis to a marked or moderate degree. The coagulation time was normal, but the bleeding time was increased slightly in three cases. In two cases the platelet count was reported and was within normal limits, and in one case the fragility of the red cells was tested and was found increased. All but one case ended in recovery.

REPORT OF CASE

An infant girl, born Oct. 28, 1927, at St. Anthony's Hospital, was noticed to have a marked pallor on the fifth day of life, which gave her a waxy appearance.

The mother, who was 38 years old, had been married two years, was in good health and had never been ill except for measles in childhood. She had had a tonsillectomy and adenoidectomy two years before examination, but no other operations. She had not had any miscarriages. The father, a coal dealer, had never been ill. They had one older child, a girl, aged 1 year and 4 months, who was in excellent health.

The infant was born by a full-breech delivery after a short labor of four hours. There was no abnormal bleeding from the mother following delivery, and the puerperium was normal. An examination of the blood of the mother was made on the seventh day, with the following result: hemoglobin content, 75 per cent; coagulation time, three minutes; red blood cells, 4,088,000; white blood cells, 10,300, and color index, 0.93. The differential count showed: neutrophilic polymorphonuclear leukocytes, 67 per cent; small lymphocytes, 25 per cent; large lymphocytes, 7 per cent, and eosinophils, 1 per cent.

The patient weighed 7 pounds, 9½ ounces (3.5 Kg.) at birth She cried immediately after birth and was not cyanosed. On the second day, a moderate

* Received for publication, July 9, 1928.

1. Ecklin: Anemia of the New-Born, Monatschr. f. Kinderh. **15**:425, 1919. Susstrunk: Severe Anemia in the New-Born, Ztschr. f. Kinderh. **38**:568 (Aug.) 1924. Donnally, H. H.: Anemia in New-Born, Am. J. Dis. Child. **27**:369 (April) 1924. Sanford, H. N.: Anemia in New-Born Infant, Am. J. Dis. Child. **30**:19 (July) 1925. Bonar, B. E.: Anemia in New-Born, Am. J. Dis. Child. **33**:226 (Feb.) 1927.

pallor was noticed which became more marked daily. On the fifth day, an examination of the blood was made. At this time, the child weighed 6 pounds, 9½ ounces (2.9 Kg.). The skin had a yellow, waxy color, but was not jaundiced. The sclerae were pale. There was no excessive nasal secretion. The tissue turgor was somewhat reduced. The child was rather listless. The pharynx and mouth were normal. Palpable lymph glands were not observed. There was not any cardiac enlargement, but there was a soft systolic murmur at the base of the heart which was not transmitted and was considered to be a hemic murmur.

The lungs were resonant throughout. The liver was palpable below the costal margin. The spleen was not palpable at any time. An examination of the blood made on the fifth day showed the following: hemoglobin content (Dare) 28 per cent; red blood cells, 1,228,000; hemoglobin index, 1.2, and white blood cells, 20,550. The differential count on 200 cells showed: neutrophilic polymorphonuclear leukocytes, 36 per cent; large lymphocytes, 26 per cent; small lymphocytes, 30 per cent; monocytes, 5 per cent; basophils, 0; eosinophils, 1 per cent, and myelocytes, 2 per cent.

There were seven neucleated red cells per two hundred white cells; these were normoblasts. The coagulation time was four minutes; the bleeding time was three minutes and thirty-five seconds.

On the seventh day, the hemoglobin content was 20 per cent; the coagulation time, six minutes; the bleeding time, five minutes and fifty-five seconds, and the blood platelets, 334,000. A fragility test done with saline solutions, varying by 0.02 per cent from 0.0 to 0.2 per cent, showed hemolysis to begin at 0.6 per cent and to be complete at 0.44 per cent, as compared to normal which begins at 0.42 per cent and ends at 0.32 per cent.

A urinalysis gave negative results for albumin, sugar and microscopic constituents. The stools were negative for blood on two examinations, and had a normal, golden yellow color. The Wassermann reaction of the blood was negative. An x-ray examination of the long bones did not reveal any syphilitic changes. The x-ray examination did not reveal cardiac enlargement.

On the sixth day, the infant who had been vomiting somewhat since the third day, began to vomit profusely after every feeding which consisted of expressed breast milk, ½ ounce (15 cc.) every four hours. On the seventh day 60 cc. of mother's blood was transfused intraperitoneally after blood grouping tests showed the blood of both mother and infant to be in group III (Jansky). On the tenth day, the hemoglobin content was 35 per cent, the red count, 1,776,000 and the white cell count, 20,300 per cubic millimeter. The differential count was as follows: neutrophilic polymorphonuclear leukocytes, 40 per cent; large lymphocytes, 24 per cent; small lymphocytes, 22 per cent; monocytes, 4.5 per cent; myelocytes, 0.5 per cent; myeloblasts, 1 per cent; basket cells, 3 per cent; eosinophils, 4 per cent, and basophils, 1 per cent.

Sixteen nucleated red cells to two hundred white cells were found; thirteen were normoblasts and three megaloblasts. The red cells showed marked polychromatophilia and anisocytosis and moderate achromia. The coagulation time was two and one-half minutes. The infant seemed more active, but she still vomited a little. On the twelfth day, she weighed 6 pounds, 11 ounces (3 Kg.) and retained almost all of her feedings. At this time, 100 cc. of mother's blood was given intraperitoneally. The infant left the hospital on the thirteenth day. She was put on a formula diet containing protein milk, dextrimaltose and spinach water, as the mother had little breast milk. The maximum amount of spinach water used was 5 ounces. No other medication was given. At the fifth week, the infant developed a rather severe jaundice which lasted for ten days. At the

fourth month, she developed furunculosis of the scalp which lasted about three weeks. The child gained weight in spite of these setbacks. When she was 7 months old she weighed 17½ pounds (7.9 Kg.), had a normal, healthy color with normal redness of lips and pink in the cheeks and was unusually active. She was getting whole milk, cereals and vegetables. A blood count at that time was not permitted, but from the general appearance of the child one could assume that recovery was complete.

SUMMARY

A sixth case of anemia of the new-born infant is reported. As in the previous cases, a cause for the anemia was not found. Regenerative changes, such as nucleated red cells, polychromatophilia and high white cell count, accompany degenerative changes, such as anisocytosis and moderate achromia. Poikilocytosis was not marked in this case. The increased fragility of the red cells suggests an inherent weakness of the cells themselves, a condition not seen in pernicious anemia or secondary anemia.

Progress in Pediatrics

EPIPHYSES

THEIR GROWTH, DEVELOPMENT, INJURIES AND DISEASES *

PHILIP LEWIN, M.D.
Associate Professor of Orthopedic Surgery, Northwestern University Medical School
CHICAGO

To the pediatrician, orthopedic surgeon and roentgenologist, the study of the epiphyses should be one of the most interesting branches of medicine and surgery. Their importance in the correct interpretation of certain conditions found in infancy and during childhood and adolescence should be emphasized. The importance in relation to general health and especially posture and scoliosis is not fully realized.

If this were an address before orthopedic surgeons, one would emphasize traumatic lesions such as "slipped epiphyses" and separation of the epiphyses, but in talking to pediatricians one does not choose to discuss at length that important phase of the subject. This paper deals primarily with epiphysitis and osteochondritis such as seen in Legg-Calvé-Perthes' disease, Osgood-Schlatter's disease, apophysitis of the os calcis, Köhler's tarsal scaphoiditis, Freiberg's infraction of the metatarsal head, Scheuermann's kyphosis dorsalis juvenilis, Calvé's vertebral epiphysitis, osteochondritis deformans juvenilis of the shoulder, of the lower end of the tibia and of the base of the fifth metatarsal bone. Epiphyseal coxa vara or epiphyseolysis and avulsion of the lesser femoral trochanter are also discussed.

The word epiphysis means an accretion, i.e., something that grows to another. (Poland) Galen distinguished between epiphyses and apophyses.

It is said that the legendary Amazons separated the epiphyses of their male children to assure female supremacy of strength and beauty. Hippocrates alluded to separation of the epiphyses.

The epiphysis is that part of the bone which is concerned with its growth, and especially with longitudinal growth of the long bones. There is at each extremity of the body or shaft of a long bone, a layer

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of cartilaginous tissue called the epiphyseal cartilage, which persists as a separate entity for a definite period, after the lapse of which longitudinal growth ceases (fig. 1).

The first stage in the ossification of the cartilage is one in which the cells enlarge and arrange themselves in rows producing a center of ossification. The matrix or ground substance in which the cells are embedded increases in quantity, and there occurs a deposition of lime salts between the rows of cells.

The functions of the epiphyses are: (1) to serve in the formation of joints, (2) to serve as attachments for muscles and tendons and (3) to develop the length of the bones.

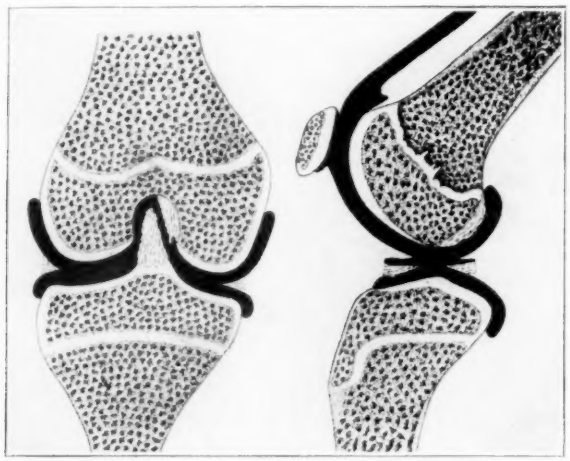

Fig. 1.—Epiphyses near the knee joint at puberty. The joint cavity is solid black, the cartilage is white and the bone shaded. The width of the joint cavity is exaggerated.

TYPES OF EPIPHYSES

Epiphyses are referred to by Parsons as pressure epiphyses, which are found at the ends of bones and transmit the weight from one bone to another, as traction epiphyses which serve as attachments for muscles and as atavistic epiphyses which represent parts of the skeleton that have lost their function. He believes that traction epiphyses were originally sesamoid structures, though not necessarily sesamoid bones; also that the anterior inferior spine of the ilium is analogous to a sesamoid in the rectus muscle attachment.

Frazer states that ossification begins constantly at one spot and at a fairly constant time in each individual bone, making a center of ossification from which the process extends. A bone may have more than one center; in fact, most bones have more than one, and some have several.

Centers may be divided into primary and secondary; the primary usually appear before birth, the secondary after birth.

An epiphysis is a part of a bone which is developed from a secondary center. It is at first separated from the main bone by a connecting area of unossified cartilage and joins the main ossification center at a later date to make the adult bone.

The epiphyseal cartilage is an important structure which lies between the bony tissue of the epiphysis and the diaphysis. In all long bones, except the fibula, the center which forms the epiphysis at the growing end and therefore joins last is the first to appear, i.e., the first to appear is the last to unite.

Sutton remarks on the disorderly manner in which centers for epiphyses appear. There are two visible at birth; one for the condyles of the femur, and one for the upper extremity of the tibia. Others appear at intervals up to the fourteenth year, when the lesser trochanter usually begins to ossify. He states that, as a rule, the centers of ossification appear earliest for those epiphyses which bear the largest proportion to the shafts of the bones to which they belong.

Delpeche's law states that excessive pressure causes an arrest or diminution of the activity of the epiphyseal cartilage and, conversely, that diminished pressure produces hyperactivity.

The periosteum is an important bond between the epiphysis and the diaphysis. The articular cartilage is the only part of the epiphysis that does not unite and become bone.

EPIPHYSEAL UNION AND AGE

Although the time of union of the various epiphyses, and the sequence of their union have long been known to bear a relationship to age, authorities have differed anywhere from three to eleven years in the dates that they have assigned for union in various parts of the skeleton. Stevenson, whose intensive study of 109 normal skeletons of which the age was known, states that the sequence of union among the various epiphyses is exactly the same in every person; and that within the limitations of the period of activity, which lies between the ages of 15 and 20, epiphyseal union is the most reliable of the various age indicators in the skeleton. With respect to age determination, the bones fall into two groups. In the group of long bones, the time of epiphyseal union is remarkably constant; in the other group made up of the innominate, scapula, ribs and clavicle, the date of union is subject to some individual variation. A single bone may tell much concerning the age of a person. For instance, in the humerus, the distal extremity unites early in the period of activity; the proximal extremity, late in that period. Accurate determination of age, however, depends on the correlation of the stages of the union found in various bones rather than on

the condition in any single portion of the skeleton. By the employment of the "epiphyseal key" that has been developed, the age at death of any person whose skeleton is preserved can be worked out. If confirmed, the importance of this work to anatomists, archeologists and medicolegal experts will be great.

In an excellent monograph on the ossification of the bones of the hand from the roentgenologic standpoint, Pryor concludes that: 1. The bones of the female ossify in advance of the male. 2. The bones of the first child, as a rule, ossify earlier than those of subsequent children. 3. The ossification is bilaterally symmetrical. 4. Variation in the ossification of bones is a heritable trait.

Based on observations on the wrists of 554 children, he summarized the chronology of carpal ossification as follows:

1. Os magnum	Female:	Between the third and sixth months
	Male:	Between the fourth and tenth months
2. Unciform	Female:	Between the fifth and tenth months
	Male:	Between the sixth and twelfth months
3. Cuneiform	Female:	Between the second and third years
	Male:	When about 3 years of age
4. Semilunar	Female:	Between the third and fourth years
	Male:	When about 4 years of age
5. Scaphoid	Female:	At 4 years of age; or early in fifth year
	Male:	When about 5 years of age
6. Trapezoid	Female:	Between fourth and fifth years (preceding trapezium)
	Male:	Between fifth and sixth years (preceding trapezium)
7. Trapezium	Female:	Between fourth and fifth years (preceded by trapezoid)
	Male:	Between fifth and sixth years (preceded by trapezoid)
8. Pisiform	Female:	Between ninth and tenth years
	Male:	Between twelfth and thirteenth years

This table is almost identical with that of Rotch, whose work was based on a study of about 1,000 cases.

According to Young, the usual appearance of centers of ossification for the tarsal bones is as follows: one for the posterior extremity of the os calcis, tenth year; one each for the cuboid, ninth month; astragalus, seventh month; scaphoid, fourth year; internal cuneiform, third year, middle cuneiform, fourth year, and external cuneiform, first year.

Gray describes the ossification of the vertebral column as follows: Each cartilaginous vertebra is ossified from three primary centers, two for the vertebral arch and one for the body. Ossification of the vertebral arches begins in the upper cervical vertebrae about the seventh or eighth week of fetal life, and gradually extends down the column. The ossific granules first appear in the situations in which the transverse processes afterward project, and spread backward to the spinous process, forward into the pedicles and lateralward into the transverse and articular

processes. Ossification of the bodies begins about the eighth week in the lower thoracic region, and subsequently extends upward and downward along the column. The center for the body does not give rise to the whole of the body of the adult vertebra, the posterolateral portions of which are ossified by extensions from the centers of the vertebral arch.

CIRCULATION

Poland says the epiphyses obtain their blood supply from the network of periosteal arteries, branches of which perforate the compact bone to be distributed throughout the cancellous bone independent of the diaphyseal blood supply. Rarely more than one or two small arteries pass over into the epiphyses from the diaphyses; this fact accounts for the infrequent occurrence of necrosis of the epiphysis when the diaphysis is more or less completely displaced from the epiphysis. Kolodny described four sets of vessels at the upper end of the femur: (1) vessels extending from the diaphysis of the femur, (2) epiphyseal vessels proper, (3) vessels arriving via the ligamentum teres and (4) periosteal vessels.

Lexer says the arteries of the head of the femur are end-arteries. Nussbaum has proved that these arteries anastomose with arteries from the fossa intercondyloidea. Bentzon states he has demonstrated that the anastomosing branches can be seen in his preparations.

Carey states that the nutrient artery is directed away from the epiphysis which unites last. Phemister found that scraping the periosteum and peeling the articular cartilage from the epiphyses was sufficient to cause cessation of growth in dogs. While workings on rabbits, Haas found that this process would hasten but not immediately effect a closure of the epiphysis. Gatewood and Mullen concluded from their experiments that immediate closure of the epiphysis can be accomplished by destroying the epiphyseal cartilage plate on the side nearest the joint.

In Carey's "Studies in the Dynamics of Histogenesis," he found that treadmill dogs mature faster than the nonrunners. Epiphyses prematurely unite in runners with resulting shorter and more condensed bone. Compression tests are higher for the bones of running than of nonrunning dogs.

He observed premature fusion of the epiphyses at the knee joint with the femoral and tibial diaphyses. In bones that have but one epiphysis, the nutrient artery is directed away from it. Correct normal muscle function is the keynote to normal formation of the bone and joint and maintenance of internal structure. The nutrient artery is directed away from the epiphysis that unites last with the diaphyses. There is no exception to this law. The epiphyses may be prematurely fused with

their corresponding diaphyses by experimental arthrodesis or increasing muscle exercise of young dogs in a treadmill (myogenic dwarfing). He stated that relatively fixed joints normally have no epiphyses.

EPIPHYSEAL DISTURBANCES

Etiology.—From the orthopedic point of view, the most important epiphyses are those of the vertebrae, hip, knee, spine, foot, elbow and wrist. The unusual epiphyses are found in the mandible, ilium, shoulder, os calcis and upper tibia.

The factors which affect the epiphyses are: heredity, circulatory changes, trauma, infection, diet, ultraviolet rays, exercise or muscular effort, fresh air, endocrine disturbances, obesity, chemicals, massage, roentgen rays and radium. The most important ones are the first seven. The three important groups of disorders are disturbances of growth and development, injuries to and diseases of the epiphyses. Interference with growth and development may be due to injury or disease of the epiphyses plus circulatory nutritional, muscular, metabolic or glandular disturbances.

In general, there is increased vulnerability of rapidly growing tissues (Jansen), and the epiphyses are in this group.

Heredity plays a part in epiphyseal disorders. These conditions are found chiefly during young childhood and adolescence. Males are more frequently affected than females, chiefly because trauma is an important factor. There may be one severe trauma or repeated slight ones. Infections of various types, including tuberculosis and syphilis, may affect the epiphyses. Nutritional disturbances are important. The effect of exercise on the epiphyses is important.[1] Glandular disturbances often affect the epiphyses, producing serious disorders. It appears that the effects of disturbances of the endocrine glands are more noticeable on the epiphyses than on the shafts of the bones. Premature ossification is found in midgets and dwarfs; delayed ossification in gigantism and infantilism. When the epiphyses of a bone have united with the shaft there can be no further increase in length of that bone (except by operation), and, conversely, until union occurs there is a possibility of increase in length. Congenital defects or absence of some of the bones of the extremities are of importance. Accessory bones, such as the scaphoids, are factors.

Axhausen believes that these conditions are due to embolism causing necrosis. Bentzon is opposed to the theory of traumatic blocking of the vessels.

1. Carey's myogenic achondroplasia is the shortness of stature due to excessive muscular effort which causes premature union of the epiphyses. He produced this condition by placing dogs in a treadmill.

Trauma may be the exciting factor in a manner analogous to bringing out the rash of measles by a hot bath. Focal infections are undoubtedly important. Under various special conditions, such as coxa plana, other theories will be given.

Experimental investigation of note has been carried out by Bentzon, Nussbaum, Phemister, Gatewood and others. Multiple epiphysitis in one person favors the theory of an epiphyseal dystrophy.

Nussbaum experimented on the upper and lower epiphyses of the femur. He cut the round ligament, then the periosteum. The center of ossification became necrosed and was absorbed, and organization of bone occurred. The lower epiphysis was detached, freed and replaced. The articular cartilage proliferated, showing that it received nourishment from the synovial fluid.

Bentzon summarized his work on coxa plana as follows: 1. It is likely that coxa plana (and other kinds of local dyschondroplasia) are caused by a lesion of the arteries of the bones. 2. The formation of cartilage in the osseous tissue and the other pathologic alterations seen in these diseases may be referred to as abnormal arterial hyperemia in the osseous tissue.

Bentzon made an anatomic study of the arteries of the bones. The course of the arteries to the head of the femur, the distal parts of the lower epiphysis of the femur, the head of the humerus and the head of the metatarsal bones is such that in young persons these arteries are especially exposed to moderate lesions (a pressure or a stretching) at a point where pressure or a blow may produce a bending of the epiphyseal cartilage (not a real epiphyseolysis). When the arteries are exposed to such a moderate injury, it is not unlikely that the vasomotor nerves in the adventitia may be damaged so that the nerves are blocked and an active hyperemia in the epiphyseal nucleus is produced.

By paralyzing the vasomotor nerves to the upper epiphysis of the femur in young rabbits and goats by periarterial injections of alcohol, Bentzon was able to produce pathologic alterations in the hips, which on histologic examinations showed a picture similar to that found in coxa plana. He, therefore, concludes that the pathologic alterations in coxa plana, osteochondritis dissecans in the knee and the head of the humerus, in Köhler's disease, and in osteochondritis of the metatarsal head may be caused by an active hyperemia produced by a moderate lesion of the arteries of the bones.

He used material obtained at autopsy and from amputations. He injected the vessels with Zinnabar-gelatin solution [2] and studied the course of the arteries by stereoscopic roentgenograms of the bones.

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2. Zinnabar (mercury sulphide) 150 Gm.; 2 per cent gelatin solution, 500 Gm. Minium (lead oxide) may be used instead of Zinnabar.

Bergmann believes that in order to explain this group of diseases of the bones one is forced to assume an aseptic necrosis, either alone or associated with another pathologic condition. Such diseases are: (1) osteochondritis deformans coxae juvenilis; (2) osteochondritis at the second and third metatarsophalangeal joints and the os naviculare pedis; (3) Kienbock's osteomalacia of the os lunatum, and (4) isolated atypical diseases of analagous character which have been found in other parts of the skeleton and to which Koenig's osteochondritis dissecans may be related to a certain degree. Finally, there belong in the classification of aseptic necrosis of the bone those processes that are sometimes seen in the course of healing of fractures of the middle portion of the neck of the femur and in traumatic separation of the upper epiphysis of the femur. His experiments were carried out for the purpose of producing nutritional disturbances in the upper end of the femur by means of various local injuries and producing bone necrosis by embolism.

In experiments on rabbits, severe dislocations of the hip joint and bloodless traumatic epiphyseal separation failed to produce epiphyseal necrosis, but after partial section of the synovial membrane in which the nutrient vessels are carried, more or less extensive areas of necrosis developed in the epiphysis of the head. These lesions were less marked when the ligamentum teres was left intact than when it was divided. Injections of suspensions of iodide of silver (from 1 to 2 cm.) into the femoral artery of the dog were without result, but injections of from 1 to 2 cm. of a suspension of pulverized metallic silver in gum arabic produced circumscribed aseptic necrosis on six occasions. The site of the necrosis was always in the diaphysis, never in the epiphysis.

Bergmann concludes that Legg-Calvé-Perthes' disease is doubtless due to an aseptic necrosis, though other factors, congenital or exogenous, may play a rôle. A purely traumatic cause of the nutritional disturbance is not probable. On the other hand, embolic occlusion of the vessels has not been demonstrated and would be difficult to explain. Presumably the entire bony epiphysis does not undergo necrosis. This assumption will explain the varying outcome of the process according to the site and extent of the necrosis. Similar considerations hold for Köhler and Kienbock's diseases. Osteochondritis dissecans is apparently often a primary aseptic necrosis with secondary separation.

Pathology.—The pathologic changes due to epiphyseal disorders concern circulatory, mechanical, traumatic, nutritional and infectious disturbances. Little is known of the pathologic changes due to epiphyseal disorders because most of these conditions do not warrant operative surgical interference, and most of them are not causes of death. One is therefore compelled to study roentgenologic evidence, experimental evidence and autopsy material, which is chronologically imperfect, as a basis for drawing conclusions.

Phemister, Kidner, Ludloff and Perthes have studied fresh cases of coxa plana. Microscopic observations have been described by various writers, including Perthes, Bentzon, Møller and Perkins. Woolf's law which applied to epiphyses as well as to bone shafts is that "every change in the form and function of the bones or of their function alone, is followed by certain definite changes in their internal architecture and equally definite changes in their external conformation in accordance with mechanical laws (Freiberg)." The application of this law is found in cases of knock knees, bow legs, vertebral kyphosis, coxa vara and other conditions.

I have studied the roentgenograms of a case of multiple osteochondritis or epiphysitis which occurred in practically every demonstrable epiphysis of the body.

Symptoms.—The symptoms of epiphysitis (excepting the acute infectious type) are similar to those of an early tuberculosis; viz.,

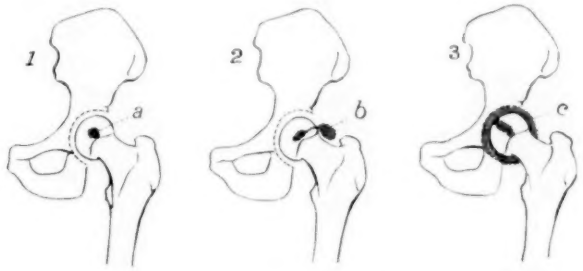


Fig. 2.—Three courses of a tuberculosis lesion in the upper femoral epiphysis; *a*, encapsulated and extinct; *b*, rupture into periarticular tissue, and *c*, rupture into joint cavity.

slight pain, limp (if a weight-bearing bone) limitation of movement and at times muscle spasm. The term "growing pains" has been placed in disrepute, but it is highly probable that congestion of the rapidly growing epiphyses may cause these symptoms and that the term "growing pains" is very satisfactory.

In various locations the symptoms are variable and are discussed in other chapters. In Still's disease there is an effect on the epiphyses which may cause early ossification and arrest of growth of the affected bones. Roentgenograms reveal changes in the shape, size and radiability of the epiphyses. A condensing osteochondritis is the most common late observation.

Diagnosis.—The differential diagnosis may be difficult. The conditions to be excluded are chiefly tuberculosis, fracture, dislocation or pyogenic infection. Syphilis, scoliosis, rickets, acute infections, congestion, or "growing pains" and Still's disease must be considered. In

other regions, hemophilia, scurvy, osteomyelitis and septic arthritis must be ruled out. In the spine, nutritional disturbances similar to those of the teeth may be found.

Prognosis and Course.—Except in cases of acute septic epiphysitis, the prognosis is usually good so far as the recovery of function is concerned, but not so good in regard to the restoration of the form of the epiphysis. The course is usually comparatively short.

In various locations the prognosis is affected by various factors. For example, in the hip, knee, or foot the matter of weight-bearing is important in the production of deformity of the epiphyses. In the spine, weight-bearing and gravity are important factors.

Treatment.—The treatment of epiphyseal disorders other than the acutely infectious type consists of general and local measures. The former are determined by the general condition of the patient, the latter are directed at the epiphyses. In general, the local treatment consists of rest, immobilization, support and relief from weight-bearing or the effects of gravity. Traction, plaster of paris casts, splints and braces are often indicated. Phototherapy, heliotherapy, active and passive movements and massage are of value in various conditions at variable periods in the treatment. The treatment should not be directed entirely to the local conditions but to the patient who has a local condition, just as the treatment by heliotherapy.

I wish to sound a warning to pediatricians concerning rest in minor conditions of the bones and joints. It is not sufficient to say "keep the child quiet." You cannot compel them to rest. They may get almost well, but in a certain percentage the condition tends to become chronic.

One of the most important prophylactic measures in arthritis deformans is the proper care of infants, children and adolescents with infectious and traumatic conditions of the joints.

Treatment in Various Locations.—Taking coxa plana for discussion, Legg is inclined to institute less active treatment than formerly. Unless there is muscle spasm, he does not prohibit weight-bearing. Calot manipulates the hip as he would a congenital dislocation and applies a cast similarly. Whitman has performed his reconstruction operation in arrested cases of coxa plana with success. Persons with epiphysitis of the spine should be treated by the nonoperative method of treatment used in early cases of tuberculosis; this practice may be somewhat of an error, but if so, it is on the side of good judgment.

OSTEOCHONDRITIS DEFORMANS COXAE JUVENILIS

Osteochondritis of the hip is known by the names of osteochondritis deformans coxae juvenilis, coxa plana, quiet hip disease, flat head or Legg-Calvé-Perthes' disease. It was described first by Legg of Boston.

It is a deforming condition of the femoral head resulting from a disturbance of growth of the epiphyseal cartilage. There is a peculiar atrophy of the epiphysis from destruction of the subchondral bony substance of the femoral head. Three factors are constant pressure, ligamentous strain and direct trauma. Various theories have been advanced by Legg, Calvé, Perthes, Waldenstrom, Jansen and Calot.

Trauma is undoubtedly an important causative factor. Infection has been ascribed as the cause, but this has not been conclusively demonstrated. Kidner and Phemister found staphylococci. The condition is predominant in the male sex, and occurs usually when the patient is from 5 to 10 years of age. It is usually unilateral, though occasionally bilateral. Roberts stated the belief that it is due to syphilis; Calot, that it is due to a congenital subluxation of the hip due to the fact that the acetabulum is shaped like a half-lemon instead of a half-orange. Legg

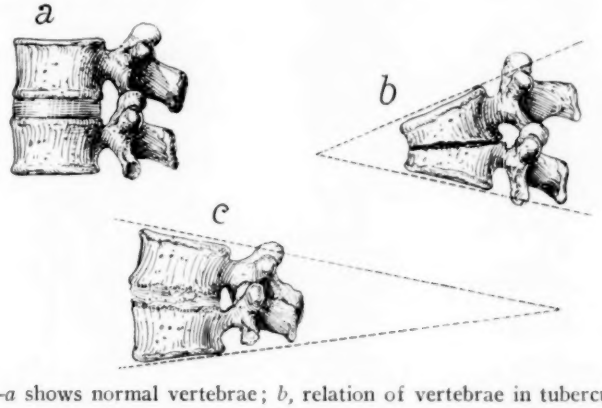


Fig. 3.—*a* shows normal vertebrae; *b*, relation of vertebrae in tuberculosis with weight borne on anterior portions; *c*, object of hyperextension with weight borne on posterior portions.

stated that it is due to interference with the blood supply. Durham and Outland said that they believed that the condition is characterized by a diminution of the serum calcium or phosphorus or both, that the pathologic process is similar to that of rickets and osteomalacia and that they may be related etiologically. Knaggs stated the opinion that it is a nonsuppurative, destructive inflammation of the bone caused by an attenuated staphylococcus.

The symptoms are limp, weakness, limitation of abduction, external rotation and shortening. Pain may be slight or absent, muscle atrophy is not marked and muscle spasm is absent or not severe. The great trochanter is prominent, and there is slight limitation of extremes of motion. Roentgenograms reveal a laminated appearance of the epiphysis. There is an irregular atrophy of the neck just below the epiphysis. Shortening and broadening of the neck are nearly always

found. Platt found the acetabulum affected in one case. Legg described the cap type and the mushroom type. Møller said that grave consequences may result, one of which is a predisposition to arthritis deformans. He offered the hypothesis of trauma as the primary cause of disturbance in the circulatory relationship between the epiphysis and the neck of the femur, the immediate result being atrophy in the former through a diminished blood supply, and hypertrophy in the latter. He believed that the hypertrophy was related to the hyperemia not only induced temporarily by the traumatic congestion, but also maintained for a considerable length of time by a propor-

Fig. 4.—Early stage of "cap" type of Legg's disease.

tionately increased blood supply, where the blocking of the epiphyseal channels distributed a heavier circulation to the diaphyseal vessels. Adding to this disturbance the factors of pressure and growth also through a definite period of time, he concludes, as to the ultimate result, that pressure on the epiphysis atrophied by diminished blood supply produced flattening; that growth, as especially stimulated in the hyperemic upper diaphysis, produced thickening in the neck and modification in shape.

Osteochondritis of the hip is a self-limited disease. The patient should be treated as though he had a mild case of tuberculosis; he should be kept in bed with abduction leg traction for from five to ten days; then a plaster of paris spica should be applied, which later should be

changed to a brace. Legg does not prohibit weight-bearing unless there is pain and muscle spasm. Mercury and potassium iodide may be given as alteratives. Phemister and Kidner have operated for this condition. Calot manipulates the hip as in cases of congenital dislocation and applies a plaster of paris cast. Whitman has performed his reconstruction operation with success in arrested cases.

In a resumé of the end-result of coxa plana, Legg stated it has been his experience that relief from weight-bearing has in no way affected end-results; that is, in those cases in which he has not allowed

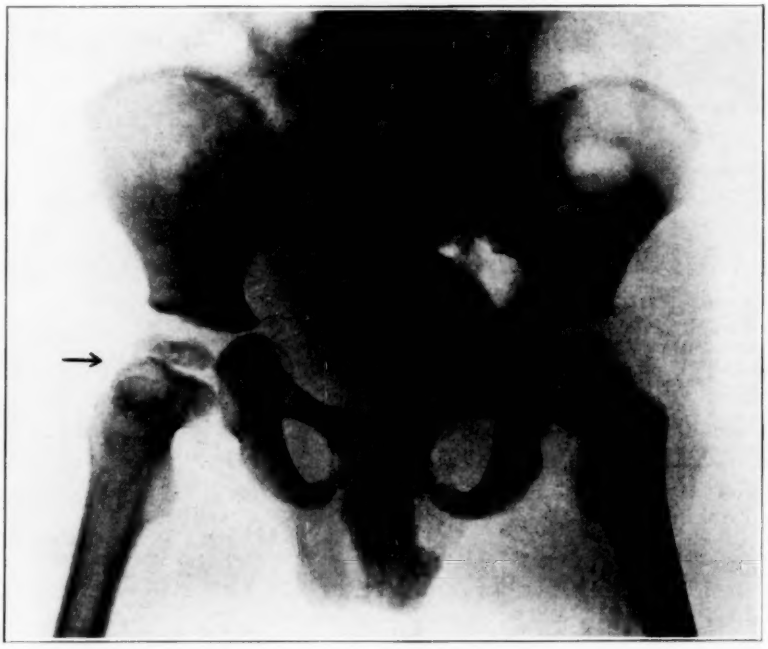


Fig. 5.—Legg-Calvé-Perthes' disease. Same case as that illustrated in figure 4, thirteen months later.

weight-bearing the end-result has not varied in any way from those in which weight-bearing on the affected leg has been allowed throughout the course of the disease. He concluded that the final results seen in coxa plana show these distinct differences in the two types of cases:

1. The mushroom type does not show marked atrophy or fragmentation of the epiphyseal bone centers. The epiphysis may migrate to the great trochanter in some cases; in others, it migrates little. Abduction and, at times, the rotations are limited when the epiphysis shows marked migration, but if there is little migration, motion at the hip may be normal in adult life. There is less shortening in this type.

2. The cap type shows marked variation in radiability in the epiphyseal bone center and neck and fragmentation of the epiphyseal bone center and marked shortening and rounding off of the upper angle of the neck. The epiphysis in some cases seems to be obliterated. The ultimate limitation of motion and shortening of the leg are generally considerable. Legg stated the belief that early in the course of the condition generally known as coxa plana one may prognosticate with much assurance what the final limitation of motion and amount of shortening is likely to be in any given case.

P. Fleming Møller compiled seventy-four cases of Legg-Calvé-Perthes' disease in which a cure had resulted, thirty-five of these being his own. The cases were classified into two groups, viz.: (1) those in which the functional result was good; and (2) those in which it was poor.

The first group comprised fifty-eight cases, or 78.4 per cent, of the total number. It represented cases in which there were no noticeable clinical changes left, beyond a slight dragging of the leg in about one half of the cases. In the second group, which comprised sixteen cases, that is, 21.6 per cent of the total, the disease had left the movement at the hip considerably restricted, as well as a permanent limp.

In seven of the cases belonging to this group, the patients had been able to get about freely, and neither the muscle spasm nor the restricted mobility prevented them from attending to their usual occupations. In the nine other cases, however, there had been not only restricted mobility and muscle spasm, but also continual pains in the hip and a reduction of the patient's working capacity.

OSGOOD-SCHLATTER'S UPPER TIBIAL EPIPHYSITIS

In 1903, Osgood reported ten cases of epiphysitis of the upper end of the tibia in boys. Several months later Schlatter described the same condition. Trauma is the exciting factor.[3] Ollerenshaw reported thirty-two cases, the majority occurring in girls. Three cases were bilateral. He states there may be seen a separation of the tibial tubercle and a fracture of the lower edge of the patella. Roentgenograms may not reveal any demonstrable lesion but usually fraying, fuzziness, or fragmentation of the tibial epiphysis are shown (fig. 6). The condition should be treated much like a fracture, viz.; a plaster cast, then a Jones knee cage with a stop joint, then physiotherapy.

In contradistinction to the treatment of a fractured patella, weight-bearing is permitted from the start. This condition is analogous to a fractured patella in an adult.

3. Delitala reported a case associated with congenital syphilis.

In the issue of *Surgery, Gynecology and Obstetrics* for July, 1928, Hawley and Griswold reported a case of Larsen-Johansson's disease of the patella. In this condition there is an anomalous bone formation, with an excessive center of ossification at the apex of the patella. These authors believe that the condition is a result of continued strain on the patellar ligaments which not infrequently occurs during such vigorous exercises or games as horseback riding, football and jumping. They believe the condition is analogous to Osgood-Schlatter's disease.

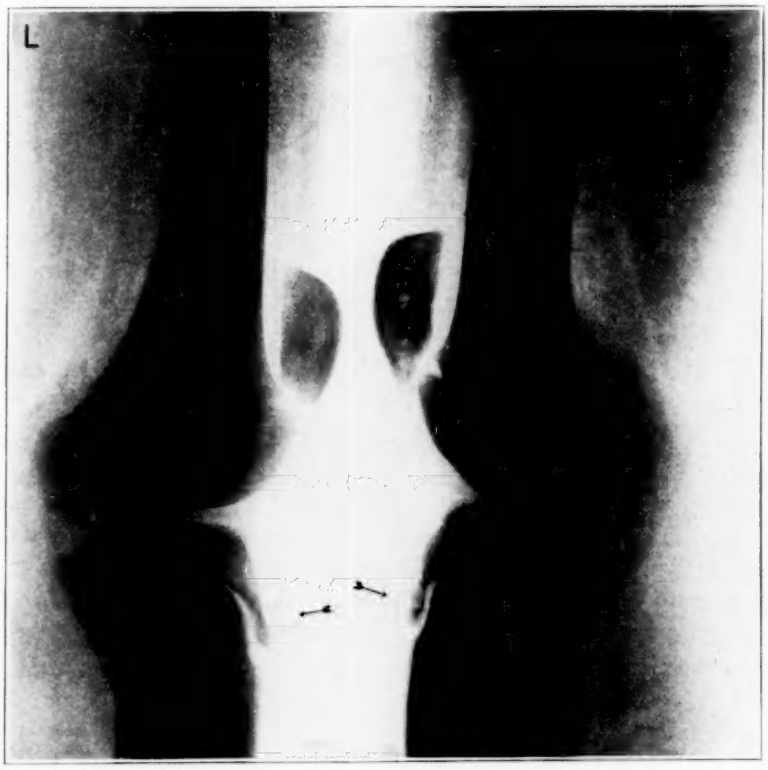


Fig. 6.—Osgood Schlatter's disease of the upper tibial epiphyses in a girl aged 12 years. She had fallen on a hardwood floor landing on her right knee. Pain appeared one week later.

OSTEOCHONDRITIS

Osteochondritis of the Upper End of the Tibia.—Ritter reported the case of a girl, 7 years of age, who, before the age of 4 years, was overweight and had extremely bowed legs. At the age of 4, one leg had become normal in appearance; the other has remained extremely bowed. The striking thing about the roentgenograms was the peculiar

condition of the inner half of the epiphysis of the upper surface of the tibia. He emphasized the similarity of this condition to that found in coxa plana.

Osteochondritis of the Lower End of the Tibia and Fibula.—In 1922, Stern demonstrated a case of osteochondritis of the lower ends of the tibia and fibula. In 1928, Ritter demonstrated a typical case of this condition in the lower end of the tibia.

APOPHYSITIS OF THE OS CALCIS

Apophysitis of the os calcis, first described by Sever, is an inflammation of the caplike epiphysis of the posterior portion of the heel bone. It is a fairly common condition, occurring usually in boys between the ages of 9 and 13 years. The probable etiology is concerned with two factors: local external and especially internal trauma, and local circulatory disturbances affecting the epiphysis during a critical period in its growth and development. The treatment consists of immobilization and relief from weight-bearing, in addition to general hygienic considerations. The prognosis is excellent. The condition is analogous to Legg's disease, Köhler's tarsal scaphoiditis, Scheuermann's vertebral epiphysitis, Freiberg's infraction of the metatarsal head, but especially to Osgood's tibial epiphysitis.

There may be a history of injury, but this is not constant. The child might have been running on hard pavements while wearing sandals or tennis shoes. The onset is insidious. Limp is usually the first symptom, and it may or may not be accompanied by pain. Pain is dull and localized to the affected area. It is less marked when the patient wears shoes with heels. Pressure from the shoe aggravates the pain. Swelling is present. There may be obliteration of the normal outlines caused by thickening of the tissues. Signs of acute infection are not prominent. Tenderness may be present over the posterior aspect of the achilles tendon, which accounts for the equinus position of the foot, and the limitation of dorsiflexion. There is a disinclination to complete the full step. Slight pronation may be present.

Roentgenograms made in anteroposterior and lateral projections may reveal irregularity of the apophysis, with thickening in all directions. Clouding, or partial obliteration of the epiphyseal line, may be observed. The epiphysis may be fragmented (fig. 7).

Diagnosis.—In the differential diagnosis, the following conditions must be borne in mind: achillobursitis, tenosynovitis, bursitis between the tendo achillis and skin, calcaneal spur, tuberculosis and pyogenic infection.

Achillobursitis, or inflammation of the bursa between the achilles tendon and the os calcis, reveals a more superficial and localized inflammation. The roentgenogram is negative for pathologic conditions of the bone.

Tenosynovitis of the achilles tendon is characterized by pain referred to the tendon and by palpable crepitus on movement. The roentgenogram is negative.

Bursitis between the achilles tendon and the skin is a superficial inflammation, usually the result of pressure of the shoe, and should be easily determined.

Calcaneal spur is rare in early adolescence, and is usually found on the inferior internal aspect of the os calcis. The area of sensitiveness

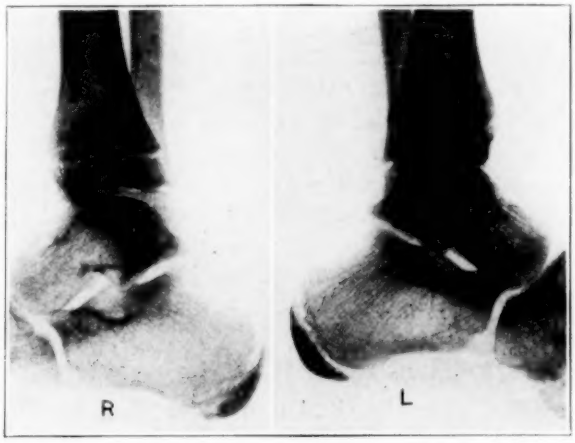


Fig. 7.—Apophysitis of the os calcis. Three weeks before the roentgenogram was taken, the patient had "turned a cart wheel," landing on his left heel. The epiphysis of the right os calcis reveals more change than does the left.

should determine the diagnosis. The inflammation is associated with the attachment of the plantar fascia instead of the achilles tendon.

Tuberculosis of the os calcis is usually in the anterior portion of the body, and not in the posterior region. Other evidences of tuberculosis are absent in apophysitis, and the roentgenogram will aid materially in the differentiation. Atrophy of the bone is not found in apophysitis.

A pyogenic infection produces more marked inflammatory reaction, with destructive osteitis.

Prognosis.—The prognosis is excellent if proper orthopedic treatment is instituted. The course is comparatively short, and may vary from a few weeks to several months. The condition may recur as a result of overactivity or trauma. Cure is effected when consolidation occurs between the os calcis and the apophysis.

Treatment.—The treatment is simple. The indications are to relieve the achilles tendon of strain and to prevent weight-bearing on the os calcis.

The most satisfactory treatment consists of the application of a plaster cast extending from the toes to just above the knee in such a manner as to hold the foot in slight equinus—thus relaxing the pull of the triceps surae—and the knee in slight flexion. Crutches should be used. This cast should be removed in two weeks, and another applied immediately extending from the toes to the garter line and holding the foot at a right angle but without varus or valgus. At the end of four more weeks, this cast should be removed and a high-laced shoe, with a ¾-inch cork lift for the heel, worn. Weight-bearing with the aid of crutches should be carried out for another two weeks. Contrast baths, baking or diathermy should be employed during this period.

During the course of treatment, emphasis should be placed on direct sunlight and proper food. If glandular disturbance is present, proper therapy should be instituted.

If the case is so mild that the foregoing treatment is not indicated, it will suffice to elevate the heel, remove the counter of the shoe and insert a pad of felt or sponge rubber in the heel. The heel may be protected by adhesive strapping, and the pronation corrected. Rubber heels should be worn.

KÖHLER'S TARSAL SCAPHOIDITIS

This condition is characterized by pain in the region of the tarsal scaphoid bone. The pain is exaggerated by weight-bearing.

This region is sensitive to movement and tender to pressure. There may or may not be a reddish discoloration and swelling. The patient limps and bears weight on the outer border of the foot to relieve the inner border. The condition may be revealed on physical examination in conjunction with the history, and is confirmed by the roentgenograms which reveal definite changes in the scaphoid. These changes consist in narrowing of the bone from front to back and condensation of the bony structure, so that on lateral view the scaphoid may look like a silver half dollar seen on edge (fig. 8). The condition is osteochondritis, and the cause has not been definitely proved. There are several theories, namely, infection, injury and congenital anomaly.

The treatment consists in the application of a plaster cast holding the foot in slight varus, the use of crutches and the prohibition of weight bearing. After a few weeks, adhesive strapping of the ankle and the midtarsal region, the use of a high-lace shoe with a Thomas heel, and the insertion of felt pads to relieve the strain on the longitudinal arch

structures, especially the scaphoid, are the measures advised. It is advisable to investigate for foci of infection, especially in the tonsils. If found, these foci should be removed. Later, flat-foot exercises, gentle massage and contrast baths are prescribed.

The disease usually occurs in young children, especially in those between the ages of 4 and 10 years. It affects boys more commonly than girls. It was originally described by Köhler of Wiesbaden in 1908.

Fig. 8.—Köhler's tarsal scaphoiditis.

Moffett, Kidner, Ely and others have written on this subject. I have observed a case of osteochondritis of the second cuneiform bone of the foot.

JUVENILE DEFORMING METATARSOPHALANGEAL OSTEOCHONDRITIS: FREIBERG'S INFRACTION OF THE METATARSAL HEAD

This condition was first described by Freiberg in 1913. He saw his first case in 1903, but his paper reporting six cases did not appear until August, 1914. Köhler of Wiesbaden described the condition in 1915, and in 1920 he reported five cases. The number of cases reported

to date is sixty-three. The two cases reported by myself bring the total number to sixty-five.[4]

Freiberg called the condition infraction of the metatarsal head. Skillern preferred the term impacted fracture to that of infraction. He called it an "egg-shell" fracture. On the assumption that it is analogous to similar conditions in other regions, especially in the hip, I wish to add the term metatarsal epiphysitis, metatarsal "flat-head" or osteochondritis deformans metatarso-juvenilis. A more descriptive term is juvenile deforming metatarsophalangeal osteochondritis.

The etiology of the condition is unknown. It is my belief that metatarsal osteochondritis has an etiology similar to that of Legg-Calvé-Perthes' disease, Osgood-Schlatter's disease, Köhler's disease of the tarsal scaphoid, calcaneal apophysitis and Scheuermann's vertebral epiphysitis. When trauma affects bone and cartilage during a period of unusual growth, the foregoing conditions may result. The important factors are: (1) trauma, (2) circulation and (3) infection.

Freiberg believes that trauma is the cause, and states that the mechanism of the injury is as follows: Under normal circumstances, the second metatarsal bone is slightly longer than the first. In the presence of a diminished power of toe flexion, especially of the great toe, it is apparent that forcible impact of the ball of the foot against the ground, not sufficiently guarded by the flexor power of the toes, will cause the distal end of the second metatarsal bone to bear the brunt of the blow. All of his six reported cases were due to trauma, especially that caused by tennis. Campbell offers the explanation that sudden jumping on the ball of the foot with the toes dorsiflexed throws the heads of the metatarsal bones downward. He thinks that basketball, tennis and running upstairs are the chief causes. Two of Painter's cases resulted from injuries received while playing baseball. Skillern's patient merely stubbed her toe.

Alberti believes in the traumatic etiology, and offered the following explanation: The second toe is longer than the others, and the head of the second metatarsal is the chief support of the foot; therefore, it is subject to greater trauma. He is of the opinion that the condition is first an osteochondritis, and then a chronic arthritis.

Axhausen is opposed to the theory of a traumatic origin, and expressed the belief that the lesion is due to an embolic obstruction of the corresponding epiphyseal endartery by tuberculous fragments or fragments with weakly virulent pyogenic cocci. The distal thickening of the shaft is explained by simultaneous emboli in the metaphyseal arterial branches, as a result of which a serious inflammation of the bone develops. The local process with secondary arthritis deformans

4. I have observed and treated six patients with this condition.

is similar to the formation of free osteocartilaginous bodies, with secondary arthritis deformans in the other joints in which the traumatic etiology has been established.

It is a condition occurring especially during adolescence. Union of the metatarsal diaphysis and epiphysis occurs between the eighteenth and twentieth years, and of the phalangeal structures, about the eighteenth year (Gray). Of the thirteen patients whose cases were reported by Panner, ten were between 10 and 14 years of age, and three were adults. If is possible that the condition in the adult patients was present but was unrecognized earlier.

Freiberg's first six patients were females. Eleven of Panner's patients were females; two were males. Two of Painter's patients were boys. Campbell's four patients were girls. All of Freiberg's cases were unilateral. One of Fischer's cases was bilateral. One of Campbell's was bilateral, the third toe of the left and the second toe of the right foot being affected. In Freiberg's six cases the second metatarsal bone was affected; one of Campbell's patients had a diseased condition of the third metatarsal bone.

Pathology, Embryology and Anatomy.—The metatarsal bones are each ossified from two centers; one for the body and one for the head of the second, third, fourth and fifth metatarsal bones. The first metatarsal bone has one center for the body and one for its base. Ossification begins in the center of the body.

The gross pathologic changes consist of flattening of the metatarsal head, with broadening of the neck and distal portion of the shaft and irregularity of the epiphyseal line. In three of Freiberg's cases, there were loose bodies.

On histologic study of two resected specimens, Axhausen found an epiphyseal wedge-shaped necrosis with corresponding reparative processes. Under local anesthesia, Unger resected the metatarsal head in one case. He found the head split, the joint capsule dense, the epiphysis soft and the marrow reddish gray. Valentin's case showed microscopically that the cartilage, and in some places the perichondrium, were rich in cells. There were no marked signs of inflammation. In the metatarsal head that Campbell resected, degenerative changes were not found.

Symptoms and Roentgen-ray Observations.—The symptomatology is brief. There is a uniform complaint of pain referred to the region of the affected metatarsal head. Swelling is usually present. It is due to exudate. A marked increase of joint tension is not demonstrable. There is a marked, sharply circumscribed sensitiveness to pressure over the metatarsal head and the metatarsophalangeal joint. Abnormal local

temperature is unusual. Definite limitation of motion with muscle spasm is present. Abscess formation has not occurred in the cases reported.

To the roentgen ray must go the credit for the recognition of this condition (fig. 9). This characteristic evidence is seen: (1) flattening of the metatarsal head, (2) broadening of the neck and distal portion of the shaft, (3) irregularity of the epiphyseal line, (4) widening of the metatarsophalangeal joint space, (5) diminished cupping of articular surface of proximal phalanx and (6) occasional line of incomplete fracture without displacement. Valentin, Axhausen and Liek found

Fig. 9.—Roentgenograms of the left foot of the patient, showing flattened third metatarsal head, broad neck and head, increased joint space and triangular-shaped area of epiphysis.

areas of sequestration similar to those observed in both cases of this report.

In view of the fact that metatarsalgia is relatively uncommon in childhood, it is advisable to have roentgenograms made of both feet of every child who has a persistent metatarsalgia. It is possible that the first film will be negative and that the examination should be repeated. Occasional roentgenograms should be made of proved cases in order to check up on the progress of the condition.

The direct diagnosis is made on the history, local examination and roentgenograms. The differential diagnosis rests between Morton's

metatarsalgia, Deutschlander's metatarsal periostitis, fracture, dislocation, syphilis and arthritis of childhood, viz.: Poncet's or Still's disease. In the condition described by Deutschlander, there is local tenderness at the junction of the middle and distal thirds of the metatarsal shaft, and roentgen-ray examination reveals evidence of periostitis. It is a subacute inflammatory periostitis.

If recognized early, and if proper treatment as outlined below is instituted, the prognosis is excellent.

The course is short, lasting a few weeks. Abscesses have not been reported. Recurrences have occurred after nonoperative treatment, and in all the cases in which operation has been performed the patients have been reported cured.

Treatment.—The treatment consists of absolute relief of the affected foot from weight-bearing by means of crutches and a block under the heel and sole of the shoe of the opposite foot. The foot should be immobilized in a plaster cast, with a small beveled felt pad applied just back of the metatarsal heads. As the cast sets, pressure is applied laterally and upward to build up the metatarsal arch. Phosphorized cod liver oil given internally is of value. Fresh air, good hygiene and food hasten recovery.

When all symptoms have disappeared, a proper shoe is prescribed. This should be a straight last, round toe, medium shank shoe into which is inserted a felt pad for the transverse arch. A metatarsal bar or anterior heel may be used, and the entire leather heel should be removed and a low rubber heel applied. A duralumin, or other metal plate made over a corrected plaster cast, may be used temporarily. Physiotherapy, heliotherapy, hyperemia and hydrotherapy are indicated after the cast is removed. Baking, gentle massage and passive and active movements with contrast baths hasten recovery. Special exercises for the metatarsal arch are performed over a round door stop screwed to a board. The patient sits with the door stops under the feet, exerting pressure back of the metatarsal heads and the toes are forcibly flexed and extended. Picking up various sized marbles from a rug, using the bare toes, and pulling objects on the floor with the toes are auxiliary exercises. Freiberg's recommendation is a felt pad to support the metatarsal head, and the insertion of a steel plate in the sole of the shoe to prevent motion at the metatarsophalangeal joints. In cases in which the roentgenogram shows loose bodies, "corpora libera," he advises arthrotomy.

Summary and Conclusions.—We have here a condition occurring more commonly in growing girls. The complaint is metatarsalgia, and the roentgenogram reveals deformity of the metatarsophalangeal joint and its component bones. The cause is bound up with three factors:

trauma, circulation and infection. It is my belief that the etiology is trauma which affects the bone and cartilage during a period of unusual growth. The condition is analogous to Legg-Calvé-Perthes' disease, Osgood-Schlatter's disease, Köhler's tarsal epiphysitis, calcaneal apophysitis and Scheuermann's vertebral epiphysitis. The prognosis is good, and the treatment consists of relief from weight-bearing.

OSTEOCHONDRITIS OF THE BASE OF THE FIFTH METATARSAL BONE

Figure 9 is a roentgenogram of the feet of a white boy, aged 14 years, referred because of pain in the region of the base of the right fifth metatarsal bone. This pain had been present for several weeks and was relieved by rest. The only significant point in the history

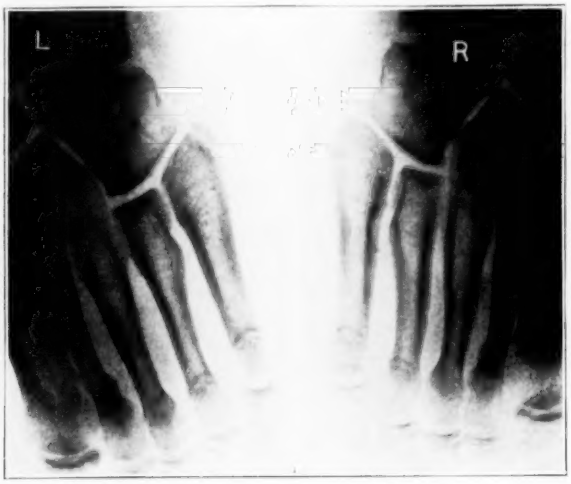


Fig. 10.—Traumatic epiphysitis of the base of the right fifth metatarsal bone.

was the grazing of the affected area six years ago when an automobile wheel ran over part of the foot.

The diagnosis of a traumatic epiphysitis was made, and roentgenograms made by oblique projection revealed almost complete absence of the epiphysis at the base of the fifth metatarsal bone (fig. 10).

A plaster of paris cast was applied, maintaining a position of eversion of the ankle and abduction of the forefoot to relax the pull of the peroneus brevis tertius muscles. At the end of two weeks the cast was removed, and the shoe was modified by the application of a reversed Thomas heel, a wedge along the outer border of the sole and the insertion of a beveled felt pad to relieve the longitudinal arch of mechanical strain.

Complete functional recovery occurred in about eight weeks. The ultimate roentgenographic appearance of the affected epiphysis is a matter of conjecture.

VERTEBRAL EPIPHYSITIS

Under the term kyphosis dorsalis juvenilis, Scheuermann of Copenhagen, in 1921, described this unusual condition of the spine. In a recent article by Calvé, two cases of another type are described, one seen by Calvé, the other by Brackett. Sorrel and Delahaye have described a similar condition. Buchman has written two important papers on this subject. Boorstein has also contributed to the literature on this subject.

The embryology of the spine offers information of interest and importance. There are two epiphyses for each vertebral body, one at the upper pole and one at the lower. These unite with the body at about the eighteenth year; therefore, epiphysitis cannot occur after that age. Before this period of fusion occurs, however, the vertebral epiphyses are subject to the same conditions as are other epiphyses.

The causes of vertebral epiphysitis are found in the following factors: (1) infection locally and remotely; (2) circulatory disturbance in the nature of embolism or thrombosis, (3) trauma both internal and external and (4) glandular disturbance affecting growth and development of the bone. The changes in the bones are those of epiphysitis. The signs of vertebral epiphysitis are similar to those of an early tuberculosis, viz.: limitation of motion, muscle spasm, military attitude, pain, tenderness and sensitiveness to jarring. Anteroposterior and lateral roentgenograms should be made and should reveal characteristic involvement in the region of the epiphysis. No exudate is seen.

The differential diagnosis is important, especially from the standpoint of prognosis. The conditions to be considered are especially tuberculosis, rickets and trauma.

Roentgenograms of a patient under my care revealed what appeared to be bilateral double transverse processes of the fourth lumbar vertebra in the anteroposterior projection; in reality, there was a fusion of the third and fourth vertebrae. In the lateral view, a definite line of fusion could be seen at the junction of the upper and middle thirds of this composite vertebra. This condition was due to epiphysitis. Tuberculosis could not be ruled out.

The prognosis is excellent if proper treatment is instituted. The course is comparatively short. Undoubtedly, many cases reported as cured tuberculosis of the spine were cases of epiphysitis.

The treatment should be the same as for mild or early tuberculosis, viz: absolute recumbency in bed on a curved Bradford or Whitman frame, with traction applied to the head or legs, or both. Immobilization is accomplished by a plaster of paris body case or spine brace. Heliotherapy is most valuable, and if it can be properly given, is probably

the only treatment necessary, except the use of a simple spine support. Good hygienic conditions must be maintained. Dietetic factors are important. If glandular disturbances are present, the patient should be treated for them. All foci of infection should be removed.

OSTEOCHONDRITIS DEFORMANS JUVENILIS OF THE SHOULDER JOINT

Figure 11 is the roentgenogram taken of an Italian child, aged 6 years, who has been under my care at various times since she was 8 weeks old. She was a full term infant, and labor had been normal. When first seen on March 19, 1920, she presented a typical case of birth palsy involving the entire right arm, with extreme ulnar deflexion

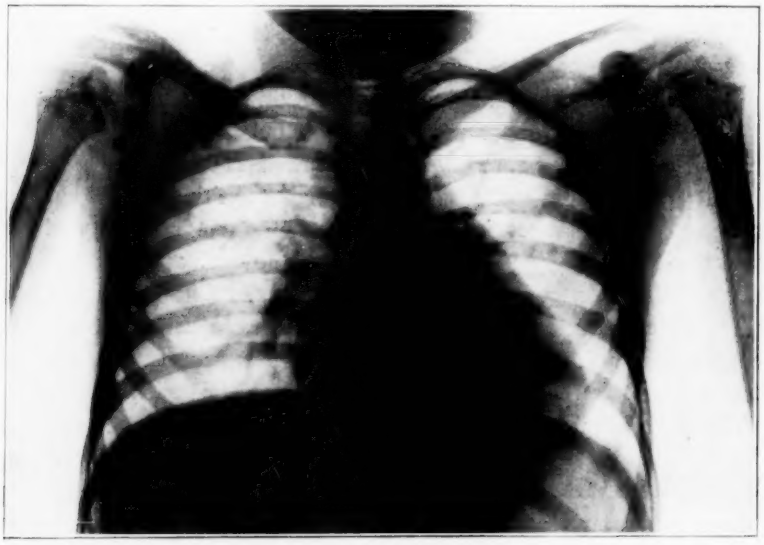


Fig. 11.—Osteochondritis deformans juvenilis of the right shoulder manifested by flattening of the medial and inferior surface of the head of the humerus with "fragmentation." The lower portion of the glenoid cavity is roughened. There is a well developed cervical rib on the right side and elevation of the scapula. A case of birth palsy.

of the hand. Roentgenograms did not reveal any demonstrable pathologic changes of the bone or joint. Treatment was instituted in the usual manner by means of a Sever type of splint holding the shoulder in abduction, the elbow flexed, the entire upper arm in external rotation, the forearm in supination and the hand in dorsiflexion. Passive movements were instituted at the outset, and as soon as the child was older, active movements were supplemented. Roentgenograms taken on Dec. 8, 1922, did not reveal any pathologic changes. A good functional

result was obtained. Roentgenograms made on Dec. 1, 1926, revealed the condition seen in figure 11. The head of the right humerus was articulating with the glenoid cavity. The noteworthy points are the flattening of the medial and inferior surface of the head of the humerus with fragmentation, and changes in the glenoid cavity. There was a well developed cervical rib on the right side, and the right scapula was elevated.

The belief is that the pathogenesis of this condition as it appears in this case is due to manipulation during the course of treatment, that

Fig. 12.—Rachitic coxa vara in a colored girl, aged 3. Two sisters were similarly affected. The gait simulated that in double congenital dislocation of the hip.

is, the forcible stretching and movements necessary during physiotherapy and medical gymnastics incident to treatment. In view of the normal birth of the infant, the possibility of instrumental or manual trauma by the obstetrician is precluded.

COXA VARA LUXANS

Coxa vara luxans is a condition seen infrequently. The clinical signs are similar to those found in congenital dislocation of the hips: limp or waddle, limitation of abduction, prominence of the buttocks and great trochanters and increased lumbar lordosis.

The etiology is a combination of heredity and nutritional disturbances similar in nature to those of rickets.

Roentgenograms reveal the diminished angle made by the neck and shaft of the femur, nutritional changes in the bones and the wide gap between the capital epiphysis and the neck of the femur (figs. 12, 13, and 14).

Fairbank described a case of coxa vara due to congenital defect of the neck of the femur. He offers the explanation that this condition is a congenital developmental error, the coxa vara deformity being secondary to this. He stated the belief that the diaphyseal spur, as

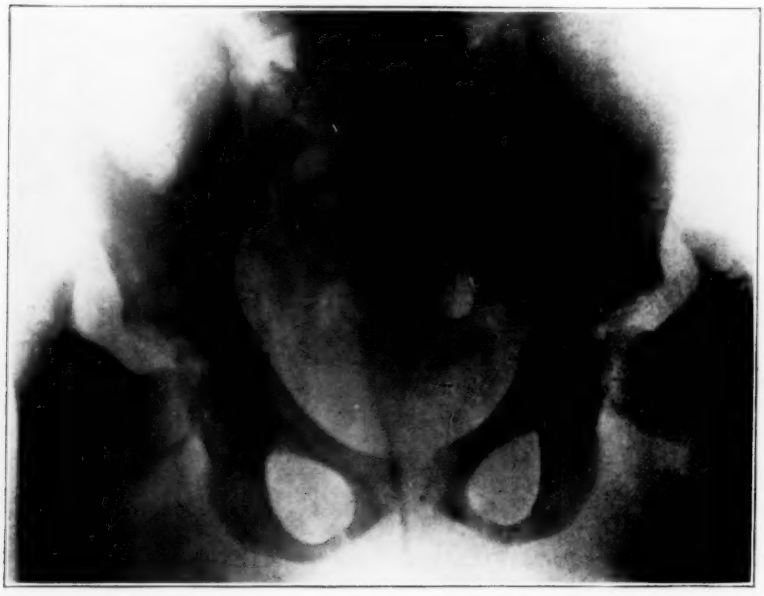


Fig. 13.—Severe bilateral rachitic coxa vara in a colored girl, aged 8 years.

Walmsley calls it, which plays such an important part in supporting the femoral head, is ossified from a separate center and not by direct extension from the shaft. It is possible that more than one nucleus of ossification may contribute to the formation of this separate fragment in some cases, since some of the roentgenograms seem to suggest this.

Coxa valga is a condition in which the angle subtended by the neck and shaft of the femur is increased above the normal. For example, the normal angle between the neck and shaft of the femur is 110 to 130 degrees; if this angle is less than 110 the condition is coxa vara, if it is greater than 130 it is called coxa valga.

I have observed several patients with cerebral agenesis in some of whom a condition of coxa valga was present.

EPIPHYSITIS

Acute Infectious Epiphysitis.—Acute infectious epiphysitis is analogous to acute osteomyelitis. It is a hematogenous infection.

The epiphyseal disk is a strong barrier or bulwark resisting the spread of infection from the diaphysis.

Chronic Infectious Epiphysitis.—Chronic infectious epiphysitis may be caused by any micro-organism, including those of tuberculosis, syphilis and coccidoidal granuloma.

Traumatic Epiphysitis.—Traumatic epiphysitis includes: separation, separation and displacement, and fracture of the epiphysis.

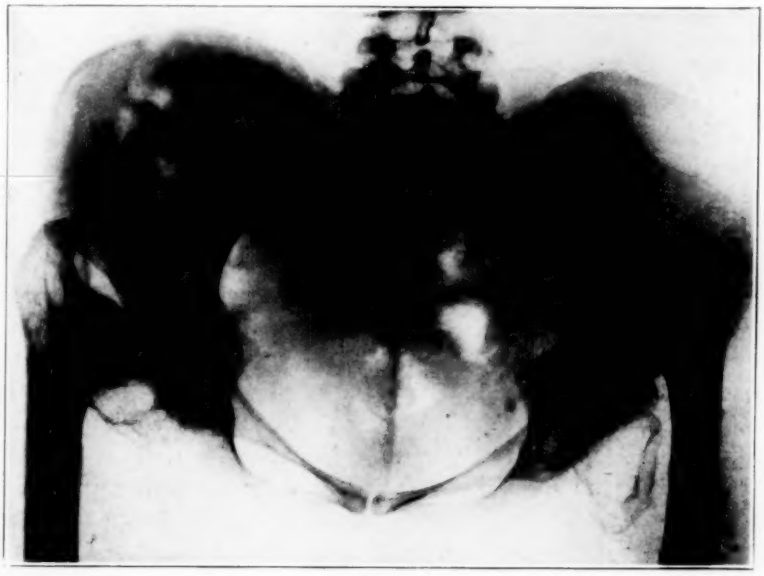


Fig. 14.—Coxa vara luxans, showing complete epiphyseal separation of the left side.

The most common locations are: the lower end of the femur, the upper and lower ends of the radius, the upper end of the femur and the upper end of the fibula.

The effect of distant trauma on epiphyseal growth is evidenced by stimulation of growth after fracture of the femur with shortening.

In the treatment of patients with congenital clubfoot, there is a traumatic effect on the epiphyses, especially on the lower end of the fibula. In the treatment of patients with congenital dislocation of the hip, there is also a traumatic effect on the epiphysis of the head of the femur.

There may be unequal growth due to disturbance of one epiphysis or part of one epiphysis.

Sylvester reports a case of syphilis in an infant, 5 weeks of age, in whom the x-rays revealed tremendous periostitis and erosion at the metaphysis, resulting in dislocation of the epiphyses. The lesion was almost completely healed after five days of treatment with sulpharsphenamine. In scurvy there may be dislocation of the epiphysis.

AVULSION

Avulsion of the Lesser Femoral Trochanter.—The ossification center of the lesser trochanter of the femur appears at about the twelfth year and unites with the shaft about the eighteenth year. It is a comparatively weak structure to withstand the considerable leverage force to which it is subjected. It is not surprising, therefore, that it is occasionally pulled off.

Practically all the reported cases have occurred in patients between the twelfth and sixteenth years. The condition is predominant in boys because of their greater subjection to trauma. The cause is always injury, either direct or by muscular pull.

The symptoms are those of disturbed function of the iliopsoas muscle: limp due to inability to flex the leg and pain and tenderness in the region of the lesser trochanter. In the standing position, the patient is able to place his leg forward, but in the supine position he is unable to lift the thigh (Ludloff). Two other signs which I have described are brought out as follows: The patient sits on a table with both legs hanging over the side. He is instructed to raise his well leg and place his heel on the table. He then attempts the same movement on the affected side, but fails. The second sign is elicited by having the patient stand squarely on both feet with knees extended. He is directed to bend from the hips and pick up an object from the floor; he is unable to accomplish this act.

Roentgenograms reveal the separation of the epiphysis of the lesser trochanter (fig. 15). The prognosis is uniformly good. The course should be considered to be from about six to ten weeks. The treatment is based on simple principles of anatomy, mechanics and orthopedic surgery. In contradistinction to the usual practice of enforcing absolute bed treatment in the normal supine position which puts tension on the psoas muscle, the patient should sit up in bed with the back rest and the pillow holding him in the position of sitting upright, with the affected thigh adducted. This position may be modified for sleeping by reducing the hip flexion somewhat, i. e., by using the back rest at 45 degrees and one pillow. As soon as possible he is put on his back on an orthopedic table, and a single spica of the hip is applied, which

retains him in a sitting position with the affected thigh adducted so that the knee passes the midline of the body. The thigh is also rotated inward slightly.

The patient in figure 15 was a boy, aged 14, who, while playing football was tackled in the region of the left hip. This caused considerable pain, but he continued to play. Several minutes later he attempted to tackle another player, but was forced to "stop short" before reaching his opponent. He felt severe pain and found that he was unable to use his left leg properly.

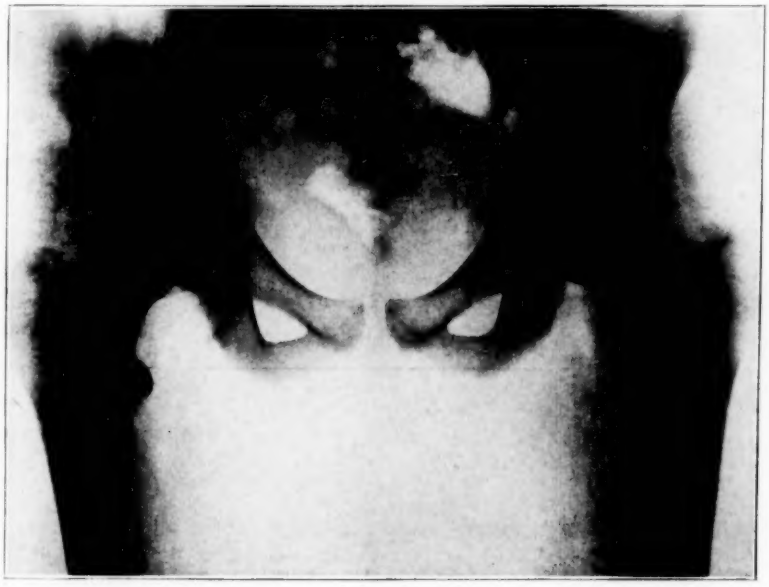


Fig. 15.—Avulsion of lesser trochanter of the femur.

Avulsion of the Epiphysis of the Tuberosity of the Ischium.—There is soon to be reported by MacLeod and myself a case of avulsion of the epiphysis of the tuberosity of the ischium (fig. 16). The condition was caused by muscular violence.

The boy, who was 17 years of age, was in a hopping race at high school. While hopping on his left foot and leg with his right leg behind, he suddenly threw the right leg into hyperextension. This act caused a sudden pain which was followed by his falling to the ground.

KIENBÖCK CARPAL SCAPHOIDITIS

This is a condition in the carpal scaphoid which is characterized by a condensing osteitis. It is undoubtedly traumatic in origin. One case

reported was due to catching a brick. Fractures of the carpal scaphoid are noted for delayed or nonunion, which undoubtedly are due to a local circulatory disturbance.

TWO STAGES OF EPIPHYSEAL GROWTH

In THE AMERICAN JOURNAL OF DISEASES OF CHILDREN for September, 1927, I described and illustrated a case of unusual roentgenographic shadows of the epiphyses, presenting the appearance of an

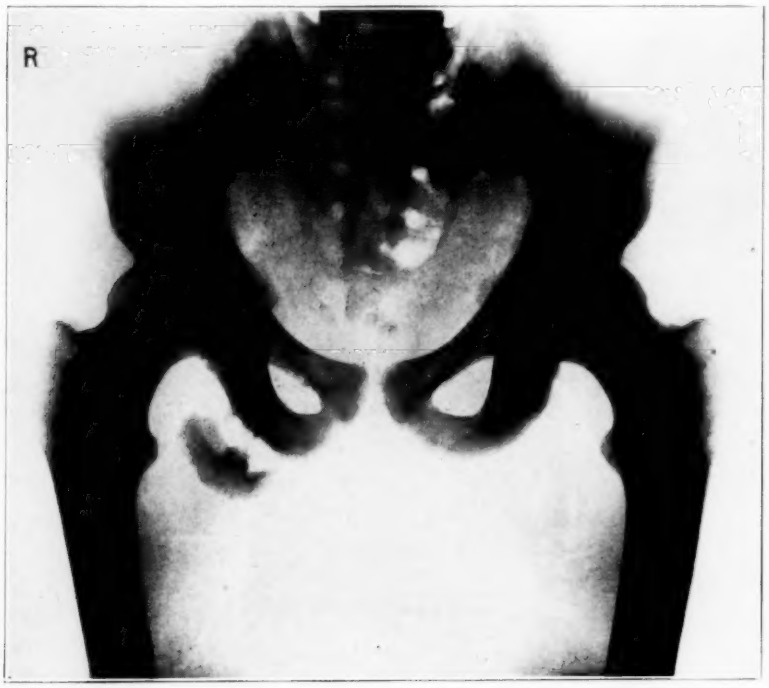


Fig. 16.—Avulsion of epiphysis of tuberosity of the ischium (MacLeod and Lewin).

epiphysis within an epiphysis. This phenomenon may be explained on the basis of a two-stage growth of the epiphysis.

The patient, D. B., was a white child, aged 2½ years, referred because of genu valgum. The only significant points in the history were as follows: He was born four weeks prematurely, and was breast fed for three and one-half months. At the age of 5 months he developed severe eczema which persisted for seven months and precluded the administration of orange juice, tomato juice, etc. He had an antipathy toward eggs. He was given cod liver oil from the fourth to the twenty-first months, when it was discontinued for three months; at

the end of this time, it was resumed. The physical symptoms of interest were moderate genu valgum and pronated feet. He has asthma at the present time.

EQUALIZATION OF LENGTH OF LEGS IN CASES OF FRACTURED FEMUR IN CHILDREN

Vernon David, in the check-up of seventy-one cases of fractured femurs in children, found that at the end of from one to two years the fractured, shortened legs were practically as long as their mates. He believed that this could not be due to stimulation of epiphyseal lines such as occurs in osteomyelitis near the epiphysis, as these fractures were not near the epiphyseal line. The overgrowth, he thought, must be compensatory and a response to the law of compensation for restoration of impaired function. The most striking instance was the presence of 2 inches (5.08 cm.) of shortening, which was reduced to 1 inch (2.54 cm.) in nineteen months.

The fact that compensatory overgrowth of a shortened femur after the fracture may be expected in a growing child is of extreme importance in further limitation of operative interference in these cases.

Whipple and Darrach had a patient who had bilateral fracture of the femurs with 2 inches (5.08 cm.) overriding on each side. Operation was performed on one side. The patient refused to have an operation on the other side, and in three years the legs were the same length.

GLANDULAR DISTURBANCES

There is undoubtedly an endocrine phase to many cases of epiphysitis and osteochondritis such as epiphyseal coxa vara or epiphyseolysis, cretinism, infantilism, gigantism, dwarfism and midgetism. It is true that one is treading on uncertain ground when one speaks of endocrine disturbances, but I am prepared to believe, although unable to prove, that there is a definite element in most of these cases.

It is difficult, and in fact impossible, to say which gland is involved in these conditions, because it is impossible to have a diseased condition of one gland of internal secretion over any period of time without disturbance of other glands as a consequence. This is due to the fact that there is a definite inter-relationship between all the glands of internal secretion.

In the condition known as dystrophia adiposogenitalis described by Froelich of Nancy, there is undoubtedly a disturbance of the thyroid and pituitary glands (fig. 17).

Dr. A. H. Parmelee will soon report an interesting and unusual condition in the crest of the ilium. A white girl, aged 5, was referred because of flat feet. She had suffered a birth injury which had caused

cerebral hemorrhage. Transfusion had been performed. Her appearance indicated mongolism; her hair was kinky and her mentality below par. Roentgenograms revealed what I have termed "onionization" of the iliac crest. There was undoubtedly a glandular disturbance in this case.

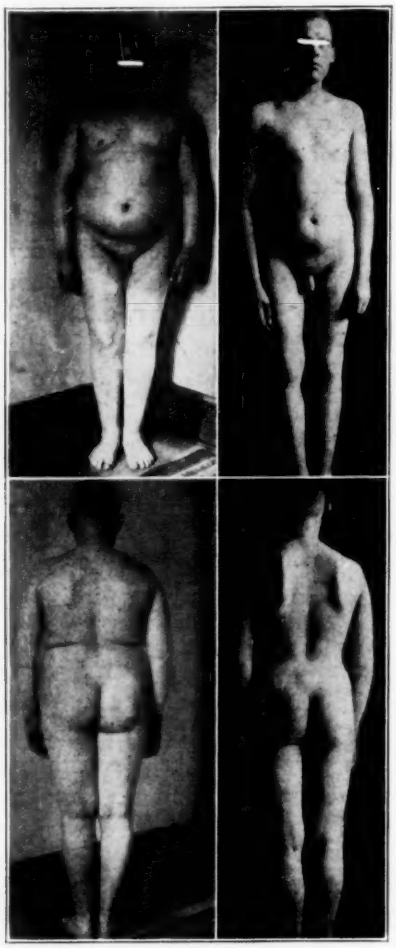


Fig. 17.—Fröhlich's syndrome, dystrophia adiposo genitalis in a boy aged 14. Showing disturbance of the pituitary, thyroid or other glands of internal secretion. Sections 2 and 4 show changes after eleven months of glandular treatment using thyroid extract and pituitary gland. The patient lost 39½ pounds (18.2 Kg.).

Englebach and McMahon stated that the general diagnostic information derived from the roentgenologic comparison of endocrinopathic and normal subjects has led them to believe that the radiologic signs offer encouraging prospects of being of more value than the basal metabolism,

chemical examinations of the blood, and other so-called specific and laboratory determinations. They believe that retardation of development of all the bones of the osseous system, not only of the carpal bones, in uncomplicated hypothyroidism can be demonstrated roentgeno-

Fig. 18.—Still's disease, arthritis deformans in a child, aged 6 years. Three days following the removal of acutely infected tonsils, a generalized arthritis appeared. Treatment consisted of recumbency on a raised Bradford frame, double spica cast wedged at the hips and knees, splints for hands, physiotherapy, massage and other measures.

logically in all ages up to that of completion of normal skeletal growth. This will be an additional aid to diagnosis in those cases already beyond

the age of normal carpal development; hitherto, the diagnosis has depended on the roentgen pictures of osseous change indicative of hypothyroidism.

Hypogonadism and eunuchoidism have consistently shown a definite late fusion of the epiphyseal ends of the long bones. While this has been suspected clinically, they are unacquainted with any definite roentgenologic demonstration of these abnormalities in secondary hypogonadism. The late closure of the epiphyseal ends in the presence of an active hormone from the anterior lobe of the hypophysis explains the overgrowth of the long bones in these subjects.

In insufficiency of the anterior lobe of the pituitary gland in which there is a primary deficiency of the anterior lobe and a secondary deficiency of the generative organs, there has been found present a late closure of the epiphyseal ends of the long bones associated with undergrowth of these bones. The reason for the undergrowth of the long bones in the presence of the open epiphyseal ends in this disorder is, in their opinion, the absence of the hormone from the anterior lobe of the hypophysis.

In the pluriglandular syndrome, the development of the osseous system as demonstrated roentgenologically is difficult to interpret. From the studies of their cases thus far, Englebach and McMahon are of the impression that the following facts obtain: (*a*) In the thyropituitary disorder there is an advance of the carpal and development of the long bone nuclei over that of pure hypothyroidism unassociated with pituitary disorder; (*b*) in pituitary thyroidism, there is a retardation of the appearance of the osseous nuclei, as well as of the fusion of the epiphyseal ends of the long bones, more marked than that in pure hypothyroidism or under normal conditions; (*c*) the markedly heterogeneous pictures presented in the multiglandular syndromes will depend on the sequence in which the various disorders were superimposed on each other. For this reason, the combination of the same glandular disorders might present entirely different radiographic pictures of the osseous development at the same age, depending on the order in which the various glands might have become involved.

In the less frequent but instructive condition of pubertas praecox (suspected pinealism), the most unusual advancement in development of the bone nuclei and early fusion of the epiphyseal lines was found. The four cases on the osseous growth and development were convincing confirmation of the exactly opposite picture consistently present in the hypogonad.

Thymolymphatism in the few cases studied apparently presented much the same osseous retardation as mild hypothyroidism. The osseous

development in positive cases of enlarged thymus should be more thoroughly studied, with a view to clearing up this mooted point of the relation of the function of the thymus to osseous development.

MISCELLANEOUS LOCATIONS AND CONDITIONS

Epiphysitis of the jaw is an important condition and is responsible for a great deal of the deformity that occurs in the lower jaws of children and adults. Like any other epiphysis, that of the jaw is subjected to trauma, infection and exposure; therefore an epiphysitis or osteochondritis may occur. This condition is responsible for the shortening of the lower jaw. Operations have been performed, and in a paper read before the American Orthopedic Association in Washington, May 1928, an oral surgeon, of Washington, described his operation of osteotomy for this condition.

Epiphysitis, or osteochondritis of the olecranon process, undoubtedly occurs, but to my knowledge has never been described. Patella cubiti is a condition described by George Gunn in *The British Journal of Surgery*. Panner's disease has been described as a condition of premature ossification of the metacarpal bone.

Osteochondritis of the ischiopubic region has been described by Valtancoli in volume 9 of *La Chirurgia degli organi di movimento* for March, 1925.

Still's disease is a condition of arthritis deformans in childhood, and definite involvement of the epiphysis occurs in this condition (fig. 18). When more is known about the gaseous exchange, that is the p_H or the C.O. balance that occurs locally in the joints, in the bones and in the epiphyses, more will be known about the pathogenesis of the conditions called osteochondritis and osteitis.

Rickets in adolescents is a condition which affects the epiphysis secondarily. Whether it is a definite condition or whether it is a "hang over" from infantile rickets is debatable. I have reported the case of a boy who at the age of 13 years had perfectly straight legs; at the age of 15 years, he had marked bowing of both lower extremities. Osteotomy was performed with a perfect result.

Infantile paralysis affects the epiphysis by its effect on the innervation of the limbs and bones. Considerable of this effect is due to its disturbance of the muscular function, which to a greater extent controls bone metabolism. I have never seen a case of "slipped epiphysis" in a child with poliomyelitis, but I have seen fractures in these cases. These fractures healed practically normally.

Coccidioidal granuloma effects the epiphysis just as tuberculosis, syphilis or any other infection does. It is characterized by the same changes that occur in tuberculosis, and in fact cannot be differentiated

clinically. This condition is known as California disease, because practically every case has come from California and especially from the San Joachin valley. There is no record of a living patient who has not suffered an amputation. I have one patient at present at the County Hospital in whom the disease began in the patella and the thumb, and there was also evidence of this disease in the lungs. For two or three years it was possible to keep this child alive without performing an amputation, but when her life was in danger, amputation above the knee was performed. She is in excellent general health and gaining in weight, and the condition of the lung has improved.

Pediatric Biographies

JAMES PRIMROSE

1580 (?)-1659

JOHN RUHRÄH
BALTIMORE

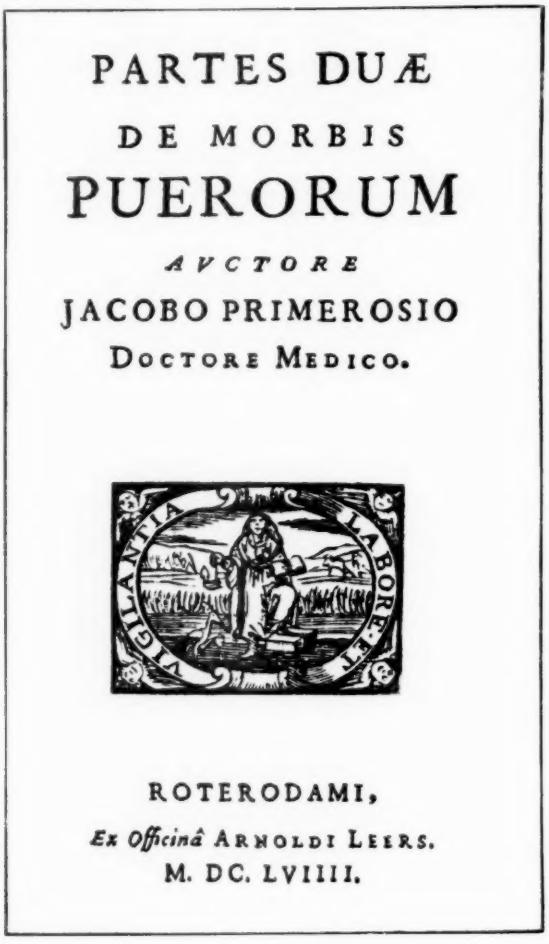
James Primrose, a somewhat prolific seventeenth century writer, is far better known as an opponent of Harvey's views on the circulation of the blood than as a pediatrician. His grandfather, Gilbert Primrose, was surgeon to James VI and his wife, Alison Graham. His father was a clergyman, who, owing to his religious views, emigrated to France. James was born at St. Jean d'Angely. He received his M.A. degree at Bordeaux and his doctorate from Montpellier in 1617. He was incorporated at Oxford in 1628 and admitted as a Licentiate of the College of Physicians in 1629. He settled at Hull, in Yorkshire, where he practiced for years, and, as Sir Anthony Wood says "was esteemed an eminent physician." He married Louise de Hankmont in 1640 at the Walloon Church in London. He died in 1659, and was buried in Holy Trinity Church in Hull.

Primrose was steeped in the teachings of the French school, which was more given to theorizing and arguing than to observation. He had studied in Paris, and as a pupil of Riolanus, professor of anatomy, he had heard Harvey's views on the circulation ridiculed, so it was only natural that he should write an essay on the subject. He liked to write, and writing, as he once admitted, was a sort of gymnastics for him. He probably added nothing to our knowledge and it is not certain that he ever tried to, but he argued and discussed so much that Haller refers to him as "contentiosus veterum defensor." Among his dozen or so better known publications was "De Vulgi in Medicina Erroribus," of which Norman Moore wrote:

> It refutes such doctrines as that a hen fed on gold-leaf assimilates the gold, so that three pure golden lines appear on the breast; that the linen of the sick ought not to be changed; that remedies are not to be rejected for their unpleasantness, and that gold boiled in broth will cure consumption.

His little book on children, "De Morbis Puerorum," was printed in Rotterdam in 1569. It is a tiny book of 125 pages divided into two parts, the first on the care of infants and the second on the diseases of children. It is a good compendium of the pediatric practice of the sixteenth century. He states that there are many causes of disease in

childhood, including among others those occurring in utero, from errors in the diet of the mother, injuries at birth, disease due to inflammation or injuries of the umbilicus, to heat and cold and bad milk. He noted that children may have the same diseases as adults as well as others peculiar to early life.


PARTES DUÆ

DE MORBIS

PUERORUM

AVCTORE

JACOBO PRIMEROSIO

DOCTORE MEDICO.

ROTERODAMI,

Ex Officinâ ARNOLDI LEERS.

M. DC. LVIIII.

Like other early writers, he follows the authorities, especially Hippocrates, Galen and the Arabians. He treats of hydrocephalus, lice, scabs and scald, wakefulness, night terrors, epilepsy, paralysis, convulsions, pain in the head, strabismus, diseases of the eye and ears and a score of other diseases, concluding with rickets. He believes this condition to be most frequent in the children of the upper classes and town dwellers, and ascribes it to their luxurious living.

The following is an example of his style:

Rhagades or cracks in the lips happen from many causes just as they do in anus, fingers, and pudenda. They often accompany indurated lips. The external causes are cold after coryza and catarrh, north wind and humors flowing over the lips. The internal cause is an acrid humor either coming down from the brain or rising from the stomach and liver. The same vapor can be active if it is acrid and ulcerative. When coction has preceded the fever they [cracks] are a favorable sign. They show that the humors causing fever are being melted and scattered. But bad cracks on the tongue, because they happen rather by the violence of the symptoms than by the strength of nature, indicate a very high temperature of the body. They happen either on account of the bitterness of the milk or hardness of the nipple or on account of the kisses of too many people. If they are to be cured by external means use chicken fat perfumed with roses and violets, fresh butter, mucilage of tragacinth, psilla, gum arabic, mastic and incense with rose water; the fat and marrow of a calf, of a goose with honey, oil perfumed with roses with the white of egg, yolk of egg, wax of the best quality, oil of turpentine, rose water ointment, white lead, camphor pomade and things endowed with slowness.

℞ adipis gallinae ℥i
olei rosati ℥ii
succi granatorum ℥i
carnis pomi cocti ℥ii

Make a liniment with sufficient oil perfumed with roses with white wax and unsalted fat.

℞ olei violatis
adipis gallinae, aut anates ana ℥ss
butyri recentis ℥i
succi plantag ℥i
cerae albae q 5 fiat linimentum.

℞ cerrissae,
amyli
cadmiae loti
lithargyri ana
Cum mucilag. gummi tragac. Vel
ciconiorum misceantur.

Add opium with milk. Cream of milk along with the fat of broth is good or mastic with white of egg according to Kuffner. If they [the cracks] come from the bitterness of the milk let the nurse be treated with a cooling diet or other things to help the milk. If from a hardness of the breasts let them be softened. Let the lips of the infant be smeared with the things mentioned above, with rose water, plantain juice, chicken fat or oil or with pomade with almond meal or with liquorice juice. Some praise omphacium [the juice of green olives] dissolved in wine, sumac, dry roses, meal of vetches with honey. Let walnuts be burnt with the hulls on and add 12 grains of peppercorns, 3 grains of incense and bruise with honey in a mortar. Let these be smeared on. You will wonder at the effect says Toletus.

NOTE.—Kuffner is probably George Khufner, who edited the book of Leonellus, already considered, and Toletus was a physician of Lyons who studied with Rabelais at Montpellier and who acted with him in the comedy of "The Man Who Married a Dumb Wife." He edited the 1538 edition of Bagellardus.

News and Comment

DIPHTHERIA IMMUNIZATION CAMPAIGN

The municipal health department and the board of education of Cincinnati are cooperating in a campaign against diphtheria in children under 10 years, to last from December 3 to January 26. Toxin-antitoxin may be administered by family physicians or district school physicians.

DIPHTHERIA PREVENTION CAMPAIGN WITHOUT CLINICS

The Detroit department of health urges parents to protect their children from diphtheria by means of toxin-antitoxin and advises them to be taken to their physician at once. There will be no clinics this year, but an intensive prevention campaign will be carried on by the physicians of the city. The Wayne County Medical Society states in its bulletin that if this campaign fails, the entire program outlined by the society "will be doomed; the free clinic will have a new lease of life, and its sponsors will have the figures to justify its existence."

DR. ABT MADE HONORARY MEMBER OF DEUTSCHE GESELLSCHAFT

Dr. Isaac A. Abt of Chicago has been elected an honorary member of the Deutsche Gesellschaft für Kinderheilkunde.

DECREASE IN PUERPERAL DEATHS

In the *Illinois Health News* it is interesting to note that the number of puerperal deaths has dropped by 9.1 per cent, or 1,141 deaths, in 1920 to 5.1 per cent, or 717 deaths, in 1927. The infant death rate per thousand has dropped materially, the decrease being most marked in the northern counties. In 1920 in the northern group of counties, the death rate per thousand was 101.5. In 1927, this had been reduced to 62.5. For the same periods for the central group of counties, the figures are 74.7 against 63.4 and for the southern group, 101.2 against 74.6.

Abstracts from Current Literature

Anatomy and Physiology

THE CLAVICULAR EPIPHYSES. T. WINGATE TODD and JOSEPH D'ERRICO, JR., Am. J. Anat. **41**:25, 1928.

1. Epiphyses may never ossify or may ossify only in part. Union of an ossified epiphysis is comparable in date and in nature with a glazing of the naked shaft end whereby its typical coral-like texture is forever obliterated. Both phenomena are types of expression of the termination of growth, but need not necessarily follow this termination.

2. The sternal epiphysis does not always completely ossify; the lateral epiphysis may not ossify at all.

3. The sternal epiphysis unites in the twenty-fifth year; the lateral epiphysis, in the twentieth year. If either end of the clavicle is naked, it glazes at the dates mentioned. Anomalies of retardation or acceleration of not more than two years do occur.

4. Sex and stock (white or American negro) do not appear to have any power of modification of these dates.

AUTHORS' SUMMARY.

THE EFFECTS OF SELECTIVE SOLAR IRRADIATION ON THE GROWTH AND DEVELOPMENT OF CHICKS. C. SHEARD and G. M. HIGGINS, Am. J. Physiol. **85**:290, 1928.

Young chicks were found to be unaffected, as regards weight, during the first two months of their life, by housing under selective filters which permitted the passage of maximal or minimal ultraviolet irradiation, or maximal or minimal irradiation with the longer wave lengths. During this period, growth was slightly greater if 2 per cent by weight of cod liver oil was added to the diet; this irrespective of their irradiation. At the end of six months, the average weight of chicks fed on standard diet and 2 per cent cod liver oil was practically the same, regardless of the light filter behind which they had been sheltered. Evidently, cod liver oil is able to induce normal growth regardless of the type of irradiation. In chicks which were housed behind blue and amber glass and fed on a diet without cod liver oil, there was a decided decrease in average weight. In such animals there was observed hypertrophy of the parathyroids, which the writers interpret as a compensatory action in the body's effort to promote normal growth; ultimately this is inadequate, and subnormal weight and signs of rickets appear.

H. E. EGGERS.

THE EFFECTS OF SELECTIVE SOLAR IRRADIATION ON THE PARATHYROID GLANDS OF CHICKS. G. M. HIGGINS and C. SHEARD, Am. J. Physiol. **85**:299, 1928.

Chicks fed with a standard diet were grown under various glass shelters which transmitted known portions of the solar spectrum. In those grown under amber and blue glass, enlargement of the parathyroids — a hyperplasia rather than a hypertrophy — was seen within the first few weeks. In chicks fed with 2 per cent by weight of cod liver oil in addition to the standard diet, the changes in the parathyroid were less conspicuous. The hyperplastic changes were shortly followed by retrogression, manifested by breaking down of the central epithelial cell cords, with increased connective tissue here, while at the same time new cells continued to be produced at the periphery. The retrogressive processes were accompanied by the formation of two types of cysts, lined either with columnar epithelium or with layers of flattened cells. Indications of the parathyroid changes were not found in the mineral content of the blood, or in the general activity.

H. E. EGGERS.

Pathology, Bacteriology and Biochemistry

A Note on a Rare Congenital Pelvic Kidney. M. B. Gilman, Anat. Record **36**:149, 1927.

A normally sized, functioning kidney in the midpelvic position was composed of three lobes, each with an artery; two lobes were supplied from the crotch of the aortic bifurcation, the other from the left internal iliac artery. The venous return was into the vena cava and left internal iliac vein. The ureter was short, 4 inches (10 cm.) in length, but coursed normally in the pelvis. Each suprarenal gland occupied the normal lumbar position, and in the absence of a normally placed left renal vein, the spermatic vein entered the left suprarenal vein. The available hospital records showed the condition had never caused trouble.

Since this segmental excretory blastema lies in close proximity to the umbilical artery and the aorta which is segmented in the embryo, the arterial supply is established to this segmental kidney. Biochemotaxis then attracts the ureter bud. The permanent functioning kidney is thus established. The venous return is established in much the same way as the arterial supply. Classification of such abnormalities and a short review of the literature are given.

The Heart of a Child, Aged 22 Months, Pressing an Anomalous Vein from the Pulmonary Auricle to the Right Internal Jugular Vein, Transportation of the Great Vessels and Left Superior Vena Cava. H. A. Harris, S. H. Gray and Caroline Whitney, Anat. Record **37**:31, 1927.

The embryologic basis of the anomalies is discussed, particularly regarding the jugulopulmonary vein. This rare vessel is shown to be a persistence of the anastomotic channels between the intestinal plexus and the anterior cardinal vein on the one hand and the intestinal plexus and the veins of the lung bud on the other. The problem of the reversal of blood flow through the persistent left superior vena cava, through the patent ductus and through the other arteriovenous shunts is considered.

A possible mechanism is suggested for the erythema and increased blood volume which is seen in certain cases of congenital heart disease. The general incompatibility between the clinical forecast and the actual postmortem observations is stressed.

The Properties of the Bactericidal Substance in Milk. F. S. Jones, J. Exper. Med. **47**:877, 1928.

Certain of the properties of the bacterial agent in milk have been studied. The substance is present in the colostrum and milk of the first few days of lactation as well as later. Its concentration varies in the secretion from various quarters of the same cow. Its activity is diminished by heat and cannot be restored again by the addition of active milk. The principle is present in whey and readily passes through the coarsest Berkefeld filter, although a considerable portion is retained by N candles. The finest filter (W) completely retains it. It is absorbed by animal charcoal but not by kaolin, kieselguhr or bolus alba. It can be desiccated, and its presence has been demonstrated in one brand of dried milk.

The Placental Transmission of Bacteriophage. John E. Blair and David L. Reeves, J. Infect. Dis. **42**:440, 1928.

It has been possible to demonstrate the placental transmission in guinea-pigs of three strains of bacteriophage of high potency, following intraperitoneal or subcutaneous inoculation. Attempts to demonstrate placental transmission of bacteriophage in which strains of low potency were used gave negative results. Experiments were negative in which the bacteriophage was administered by mouth, although it was shown that feces of the mother contained the bacteriophage immediately after feeding.

Authors' Summary.

COMPOSITION OF BONE: 1. ANALYTICAL MICRO-METHODS. 2. PATHOLOGICAL CALCIFICATION. 3. PHYSICOCHEMICAL MECHANISM. 4. PRIMARY CALCIFICATION. 5. SOME PROPERTIES OF CALCIUM CITRATE. M. J. SHEAR and BENJAMIN KRAMER, J. Biol. Chem. **79**:105 (Sept.) 1928.

The first article describes a technic for determining the carbon dioxide content of bone which requires about 20 mg. of bone powder, and the content of calcium and inorganic phosphorus which requires 10 mg. of bone powder. By this method, seven kinds of pathologic calcified tissues were analyzed: thyroid and fibroid and those of tuberculous lymph nodes, aortic cusps, the splenic capsule, lymph nodes of the lung and mesenteric lymph nodes. All these tissues gave normal values for the ratio of residual Ca:P. No satisfactory evidence was found in bones of the presence of a compound with the formula $Ca_3(PO_4)_2$. Inorganic solutions of serum with empiric Ca x P products amounting to less than 30 appear to be undersaturated with respect to $CaHPO_4$; calcification is not obtained with these solutions. The evidence shows that rachitic serum is definitely undersaturated and that normal serum is slightly undersaturated with respect to $CaHPO_4$. The proportion of carbonate in the bone of normal rats increases with age. The ratio of carbonate calcium to the total calcium is about 8 to 10 per cent in the bones of young rats, and 15 to 16 per cent in those of adult rats. The proportion of carbonate in the bone of rachitic rats is greater than that in the bone of normal rats of the same age. The ratio residual Ca:P in primary calcification has a high value. This high ratio is interpreted to indicate the presence of a basic calcium salt in freshly deposited bone salts. The composition of the primary calcification appears to be independent of the antirachitic agent. High Ca:P ratios were obtained regardless of whether the fresh calcification was induced by concentrated cod liver oil, butter, irradiated cholesterol or irradiated yeast. The deposition of bone salts appears to be dependent on physicochemical equilibriums existing in the serum. The rôle of citrate may be important in calcification. Titration of the conductivity of sodium chloride with sodium citrate at 25 C. gives results which are normal and in agreement with calculated values. Similar titration of the conductivity of calcium chlorid with sodium citrate gives abnormal results. These observations are direct evidence of the binding of calcium ions by sodium citrate in some kinds of soluble complex.

SANFORD, Chicago.

THE HYDROGEN-ION CONTENT OF VACCINE LYMPH AND ITS RELATION TO THE POTENCY AND KEEPING PROPERTIES OF LYMPH PREPARED UNDER TROPICAL CONDITIONS. J. CUNNINGHAM and K. S. MHASKAR, Indian J. M. RESEARCH **15**:819, 1928.

The chemical reaction of vaccine lymph prepared and stored under tropical conditions has been investigated. Glycerinated lymph was used for the tests. Dialysis and centrifugalization were used to obtain a clear fluid for test purposes. In thirty-five freshly prepared batches of lymph the p_H varied between 7.2 and 8, the majority lying between 7.4 and 7.8. After exposure to room temperature (98.4 F.) for varying periods, the majority of lymphs became more acid. At the same time there was a great reduction in the numbers of bacteria. The same tendency to an increased acidity was seen after the lymphs were treated with chloroform vapor for purposes of purification. When the reaction of different samples of the same batch of lymph were artificially adjusted to p_H 4, 6, 8 and 10 and then stored at 55 F. and room temperature (average 98.4 F.) for different periods, it was found that the sample in which the reaction was adjusted to p_H 8 gave the best results. The investigation shows that there is a tendency in most lymphs in the tropics to become more acid on storage or exposure, and, as the formation of acid has a deleterious action on the vaccine virus, the authors recommend that the reaction of each batch of lymph should be carefully adjusted to a point which is definitely alkaline, say p_H from 7.6 to 7.8, to guard against deterioration from this cause.

AUTHORS' SUMMARY.

DIVERTICULUM OF HUMAN HEART. M. R. DRENNAN and G. T. VAN DER VIJVER, South Africa M. J. **2**:58, 1928.

A case of sudden death from the rupture of a ventricular diverticulum of the heart is reported in a child, aged 4 years. The condition found seemed to indicate that the vortex of superficial muscle fibers at the left apex may be a weak spot at which a diverticulum may form. In the case described there was no valvular or other cardiac lesion that could have caused chronic strain on the muscle of the heart.

[ARCH. PATH.]

THE RELATIONSHIP BETWEEN THE DEXTROSE OF THE BLOOD AND THE SPINAL FLUID: ITS DIAGNOSTIC VALUE. S. KATZENELBOGEN and M. STOILOFF, Ann. de méd. **23**:160 (Feb.) 1928.

The normal quotient "dextrose of spinal fluid: dextrose of blood" is, according to Derrien, approximately 0.5. In other words, the content of dextrose per cubic millimeter of blood is twice as high as in the same amount of spinal fluid. An increase of this factor points to an increased permeability of the meninges for dextrose, and vice versa. Other authors report similar values with the exception of Polonowsky and Duhot, who found a normal quotient of 1.

The results obtained in different diseases are condensed in the following:

Purulent meningitis	0.05—0.30
Cerebral abscess (with purulent spinal fluid)	0.27—0.34—0.36
Mental disease	0.51—0.74
Other diseases of the nervous system	0.53—0.82
Different other diseases	0.41—0.83

The values for the dextrose quotient of the spinal fluid and the dextrose of the blood are similar in different diseases and do not help in establishing a differential diagnosis.

WEIL, New York.

THE EFFECT OF ULTRAVIOLET LIGHT ON THE NUTRITION AND METABOLISM OF THE CHILD: THE MELTING POINT OF ERYTHROCYTES BEFORE AND AFTER IRRADIATION. E. RULLMANN, Arch. f. Kinderh. **84**:183 (June 15) 1928.

In a continuation of his extensive study with ultraviolet ray therapy, the author tested the melting point of the red blood cells in both physiologic sodium chloride solution and in 9.4 per cent dextrose solution, before and after ultraviolet irradiation. Six cases of hilum tuberculosis showed an increase in both solutions in practically all trials. The average difference was about 1 degree more after irradiation. The irradiation lasted for from twenty-five to sixty minutes, although the length of time apparently did not have any effect. The average temperature required was 70.5 before and 72 after irradiation. In one case of diabetes mellitus the result was approximately the same. In the last case, one of rickets and anemia in a child, aged 8 years, the temperature varied considerably. Of seven cases, four showed a lower and three a higher temperature after irradiation than before; the difference in both averages was less than 0.5 degrees.

SANFORD, Chicago.

THE EFFECT OF HYPERTONIC DEXTROSE SOLUTIONS ON THE EXCRETION OF WATER AND CHLORIDES BY THE KIDNEY. J. M. GOLDBERG, S. M. GAMEROW and M. L. PINCHASSIK, Biochem. Ztschr. **199**:107 (Aug.) 1928.

The authors injected 10 cc. of 50 per cent dextrose solution into the jugular veins of rabbits under ether narcosis. Specimens of blood, liver and muscle were taken before and ten, twenty and twenty-five minutes after the injection. There was a slight increase in the water content of the blood and liver, while that of the muscle was decreased. Variations in the chloride content of the three

tissues were slight and inconstant. The total daily volume of urine was measured following from five to fifteen daily injections of hypertonic dextrose solutions (10 to 50 per cent). There was usually a decrease in the excretion of urine. When the injections were stopped, the volume of urine excreted increased.

BRAHDY, New York.

THE LOCUS OF THE ANAPHYLACTIC REACTION. T. EHMER and J. HAMMERSCHMIDT, Klin. Wchnschr. **7**:931, 1928.

As a result of a specific septicemic infection in mice, a total but selective blockade of the vascular endothelium of the closed blood channels is accomplished, and anaphylactic shock in these animals is completely suppressed. This means that the vascular endothelium comes into consideration as a consequential tissue for anaphylactic shock. Further, there is no inhibiting substance in the blood of such infected animals, and anaphylaxis with septicemias by organisms which do not block the endothelial cells is not suppressed. Finally, the primary serum toxicity of foreign serums does not affect the vascular endothelium.

AUTHORS' SUMMARY.

AN ATTEMPT TO EXPLAIN THE MECHANISM OF SPONTANEOUS HEMORRHAGES IN SCURVY. W. M. NOWODWORSKI, Ztschr. f. d. ges. exper. Med. **58**:424, 1927.

In fourteen cases of scurvy, the number of blood platelets was somewhat decreased (average, 60 per cent of the normal value); there were no changes in clotting time; calcium and magnesium contents were somewhat decreased. The values for fibrinogen and for thrombin were within normal limits. Contractibility of the clots was normal. The author believes that the cause of spontaneous hemorrhages in scurvy lies in changes of the vessel walls.

B. LUCKÉ.

THE SIGNIFICANCE OF HEXOSEDIPHOSPHORIC ACID AND DIPHOSPHOGLYCERYL ACID IN CALCIFICATION OF THE SKELETON. HERMANN MAI, Ztschr. f. Kinderh. **45**:653 (June) 1928.

Sodium hexosediphosphate is split by the growing skeletal tissue to a much greater extent than in adults. This increased availability of inorganic phosphates meets the increased need in the growing bone system. As earlier results indicate, rachitic skeletal tissue splits hexosediphosphoric acid more strongly than does nonrachitic skeletal tissue. The optimum reaction of hexosediphosphatase, which is scant in growing tissues, diminishes with an increase of acidity. Skeletal material of young cattle causes cleavage which is analogous to that in man more strongly than the tissue of grown animals. The diphosphoglyceryl acid, newly discovered by Greenwald and Jost and existing especially in red blood corpuscles, is split only to a vanishingly small degree by skeletal material in vitro. Its importance in metabolism is that inorganic phosphate already split in the blood may be supplied to the calcifying tissue. An optimum for cleavage cannot be definitely demonstrated for diphosphoglyceryl acid.

THE CAUSE OF THE SLOWING OF THE GLYCEMIC REACTION BY THE WHEY OF COW'S MILK. E. HOLZMANN, Ztschr. f. Kinderh. **45**:720 (June) 1928.

Welcker and Jäger seemed to show that with the addition of 0.057 per cent of secondary sodium phosphate, the amount of phosphate in human whey would be increased to that of cow's whey; further, the difference between the effect of cow's whey and human whey on the blood sugar curves would disappear. They concluded that the effect was due to the difference in the content of phosphate, a rich content causing a slower absorption in the intestine. If cow's whey, moreover, were deprived of its albumin, an equal amount of phosphate was removed

and the whey no longer acted as a deterrent. Holzmann found, however, that the removal of phosphate from cow's whey in this manner still left twice as much as in human whey without any effect on the glycemic curve; that is, the difference in phosphate content was not adaquate to account for the change. Then cow's whey was separated from its albumin; after restitution of the 15 per cent of phosphate lost with it, 0.3 per cent of albulactin, a dried preparation of the albumin of cow's whey, was added. Outside of albulactin, there was nothing in this mixture to retard the glycemic reaction. There was a slowing, but not so great as with the whole cow's whey. The result was the same when the process was carried out quickly with all the components fresh. On the basis of his experiments, Holzmann, therefore, cannot agree with Welcker and Jäger that differences in the action of the two wheys can be laid to a difference in phosphate content; he ascribes it to both the albumin and the salts. EMERSON, Boston.

THE ANTIGENIC PROPERTIES OF ANATOXIN. M. ISABOLINSKY and W. GITOWITSCH, Ztschr. f. Immunitätsforsch. u. exper. Therap. **52**:334, 1927.

The authors maintain that the combining properties of anatoxin signify more than precipitability. Anatoxin retained its immunizing property for one year. For the preparation of anatoxin it is best to use an old toxin which possesses a good combining power, a more important factor than toxicity. The use of 5 per cent formaldehyde in the production of anatoxin is advantageous in that the vessel containing the mixture can be frequently opened without danger of bacterial contamination.

THE ACTION OF DIPHTHERIA ANTITOXIN IN VITRO AND IN VIVO. BECKER, Ztschr. f. Immunitätsforsch. u. exper. Therap. **52**:402, 1927.

Toxic diphtheria bacilli growing in diphtheria antitoxin rapidly become less toxic or lose their toxin forming power entirely. Normal serum injected simultaneously with washed toxic diphtheria bacilli does not affect the infection of guinea-pigs; one-tenth unit of antitoxin hinders the infection slightly, one unit decreases it distinctly and ten units prevents its effects. Antitoxin (ten units) injected twenty hours after infection shortens the course and if given forty hours after the infection is still able to cure. The presence of antitoxin stimulates the auto-immunization of the infected animal. PAUL R. CANNON.

LIPOIDS IN THE LIVER AT BIRTH. S. NUNOSE, Japan M. World **8**:8, 1928.

In the still-born, the amount of neutral fat is larger than in the infants born alive; it is also more evenly distributed in the cells of the lobules, and is found hardly at all in the Kupffer cells. By Ciaccio's method, a positive reaction was obtained oftener in the still-born than in those born alive. It is suggested that these differences in the distribution of lipoidal bodies may have medicolegal value.

[ARCH. PATH.]

DOES THE PANCREAS OF INFANTS DIGEST THE NUCLEI OF CELLS? J. LUKÁCS, Orvosi hetil. **72**:496, 1928.

The author tries to answer this question through physiologic experiments. Finely cut calf's liver in tiny bags made of gauze was fed to infants aged from 6 to 12 months. These bags were recovered from the stools, and their contents were examined. Adults and older children digested the nuclei completely, while infants showed an incomplete digestion. Experiments in test tubes were carried out by mixing finely ground pancreas tissue obtained from autopsies with liver suspension. The results again showed that the infantile pancreas cannot digest nuclei. ZENTAY, St. Louis.

Nutrition

THE ANTIRACHITIC EFFICIENCY OF SKYSHINE IN WASHINGTON, D. C. WILLIAM D. FLEMING, Mil. Surgeon **63**:658 (Nov.) 1928.

The light received from the north sky (skyshine) without direct sunlight in Washington, D. C., during the months of April, May, June and July, 1928, afforded a sufficient number of ultraviolet rays to promote normal ossification in rats which were confined under a glass permeable to ultraviolet light to a degree of about 29 per cent. These rats were on the diet that produced marked rickets in rats which did not receive ultraviolet light under window glass. The gain in weight of the rats receiving this amount of ultraviolet light was also greater than that of rats kept under window glass. It appears, therefore, that a solarium designed for ultraviolet therapy and glazed with a glass permeable to ultraviolet light to the degree of at least 29 per cent need not be placed on the south side of a building where it will receive direct sunlight. As far as antirachitic therapy is involved, it will be effectively placed if it receives the light from only the northern hemisphere of the sky.

SPECIFIC DYNAMIC ACTION OF FOODSTUFFS IN CHILDREN. E. HELMREICH, Arch. f. Kinderh. **84**:194 (June 15) 1928.

In an earlier issue of the *Archiv für Kinderheilkunde* (**83**:193 [Feb.] 1928) Hilsinger reported the cases of three children in whom the specific dynamic action of milk and meat was tested. He found that the specific dynamic action decreased after from five to seven hours and then increased without reaching the fasting level. Helmreich tested eighteen children from 3 to 14 years of age. In children aged from 3 to 5 years, the specific dynamic action varied from 0.38 to 5 calories. In the older children it was higher; in one child, aged 14 years, it was 33 calories. The author does not agree with Hilsinger in his statement that characteristic differences in race could be determined by the reaction time of specific dynamic food action.

SANFORD, Chicago.

TREATMENT OF INTESTINAL DISTURBANCES BY THE USE OF A GARLIC PREPARATION (KNOBLAUCH). ERBACH, München. med. Wchnschr. **75**:87, 1928.

The author, on giving a garlic preparation, observed a marked change in the intestinal flora and a decrease in motility which resembled a narcotic in action. His conclusions are based on the treatment of fifty patients with acute and subacute intestinal catarrh. Two tablets were given from three to four times a day; and within forty-eight hours the consistency of the stools became normal. The appetite quickly became normal.

CHILDREN WITHOUT AN APPETITE. FRANZ HAMBURGER, München. med. Wchnschr. **75**:1459, 1928.

The author gives a lengthy, complete summary of the loss or absence of appetite in children.

The article should be read to be appreciated; and a translation in the form of a monograph might be of great help in instructing physicians and mothers when this annoying condition exists.

SCHORER, Kansas City, Mo.

SIMPLE PREPARATION OF EIWEISSMILCH AND BUTTERMILK IN THE HOUSEHOLD. GÉZA KRAUSZ, Ztschr. f. Kinderh. **45**:686 (June) 1928.

Buttermilk may be prepared by any housewife in ten minutes, according to Krausz, in the following simple fashion: A liter of whole milk (3.3 per cent protein, 3.7 per cent fat and 5 per cent lactose) is coagulated with 8 cc. of a 75 per cent solution of lactic acid and cooked a short time. By this method, the

casein and practically all the fat are precipitated in big curds. The milk is strained through a cloth and allowed to drain for five minutes. A fourth, or about 20 Gm., of the protein coagulum is mixed with 20 Gm. of calcium caseinate (Stoeltzner's casein calcium) and a small quantity of water and passed through a fine sieve into the whey. Penetrated by the calcium caseinate, the coagulum is finely divided; on the other hand, the calcium caseinate is held in suspension by the adhesive strength of the coagulum. For a finer division, the whole mixture is put through the sieve a second time and increased to 1 liter with the addition of water. The mixture now contains 9 Gm. or 0.9 per cent fat, 28 Gm. or 2.8 per cent protein and 50 Gm. or 5 per cent sugar. Eiweissmilch is prepared in a similar manner. Two thirds of the coagulation of casein is mixed to a paste with 10 Gm. of calcium caseinate and water is substituted for one half of the whey. The mixture then contains 24 Gm. or 2.4 per cent fat, 32 Gm. or 3.2 per cent protein and 25 Gm. or 2.5 per cent sugar.

EMERSON, Boston.

TREATMENT FOR RICKETS WITH IRRADIATED ERGOSTERIN PREPARATIONS. A. FLESCH, Orvosi hetil. **72**:828, 1928.

The author conducted his experiments during the winter and early spring, in order to exclude the possibility of spontaneous improvement. He used Merck's Vigano, Arnea's Viosterin and a Hungarian preparation. The results are satisfactory, as the patients with rickets and tetany improved promptly under the treatment. The ergosterin seemed to have a more prompt action than cod liver oil. The reason for this is that 20 Gm. of cod liver oil contain only 1 mg. of vitamin. A large quantity is required, therefore, for prompt action and, besides, cod liver oil has a variable content of vitamin. When one compares the results with those obtained by quartz light, with the exception of persons with eczema, ergosterin seems to have about equal values.

ZENTAY, St. Louis.

REGULATION OF THE BLOOD SUGAR IN NORMAL INFANTS AND IN INFANTS WITH EXUDATIVE DIATHESIS. C. W. HERLITZ, Acta Paediat. **7**:1 (May 15) 1928.

In determinations of the blood sugar during fasting in seventy-eight normal infants ranging in age from 1 to 11 months, Herlitz found an average value of 0.087 per cent, with a range of 0.071 to 0.103 per cent, by the Hagedorn-Jensen method. Patients of the same age but showing eczematous eruptions or other evidences of exudative diathesis had a high normal or supernormal percentage of blood sugar during fasting, if the eruption had been present less than two weeks; on the other hand, the level was normal when the skin manifestations had been present for more than two weeks. In the following respects also, the patients with fresh eruptions differed from the normal group and from those with an eruption of long standing: the peak of the blood sugar curve after oral administration of 1.5 Gm. of dextrose per kilogram of body weight was unusually high; after subcutaneous administration of 0.3 Gm. of dextrose per kilogram of body weight, not only was the peak of the blood sugar curve high but the duration of elevation of the blood sugar level was prolonged; after oral administration of levulose, the concentration of levulose in the blood at the end of an hour was abnormally high. With the healing of the eruption, such abnormalities of the blood sugar-regulating mechanism vanished.

Herlitz ascribes these phenomena to the presence of the eruption, which increases the tone in that portion of the autonomic nervous system which controls the carbohydrate metabolism of the liver. He submits evidence from the literature to support his assertion that the exudative diathesis is accompanied by an increased irritability of the entire autonomic system.

The article is in German and is accompanied by a valuable bibliography on dextrose tolerance tests in infants.

MCINTOSH, Baltimore.

QUALITATIVE AND QUANTITATIVE UNDERNOURISHMENT IN THE BREAST-FED INFANT. M. F. RADNEFF, Russian J. Pediat. **12**:100, 1928.

Undernourishment is responsible for many nutritional disturbances of infancy; 96 per cent of all cases of dystrophy are due to undernourishment, while only 4 per cent are due to overnourishment (Ribdeau-Dumas). Mothers who are on insufficient diets during the last part of pregnancy will show a decrease in the quantity as well as in the quality of their milk. The author reminds the reader of the fact that undernourishment may also cause vomiting (Vomissement par inanition of Lereboullet) as well as diarrhea in the infant.

The protein of the milk may be present in sufficient quantities; yet, if there is an insufficiency of certain amino-acids, definite disturbances will take place. Insufficiency of lysin will lead to insufficient growth of the body and insufficient tryptophan to no gain or loss of body weight. The avitaminoses are then considered.

THE USE OF PROFESSOR KRASNOGORSKY'S GASTRIC ACID MILK MIXTURE IN NUTRITIONAL DISTURBANCES. H. P. SHASTEEN, Russian J. Pediat. **12**:109, 1928.

Professor Krasnogorsky advised the author to use milk acidified with the natural gastric juice, which was obtained from the institute of experimental medicine of the University of Leningrad. Gastric juice is preferred to the use of other acids (such as lactic, hydrochloric and citric) on account of the presence of ferment in it. The stock mixture is prepared as follows: 500 cc. of whole cow's milk is added to 350 cc. of a 10 per cent strained gruel (rice), 150 cc. of the natural gastric juice and 50 Gm. of sucrose. In some cases, skimmed milk is used instead of whole cow's milk. The use of 5 per cent of gastric juice in the mixture results in a hydrogen ion concentration of 5.93; of 10 per cent gastric juice, 5.54; 15 per cent, 4.96 and 20 per cent, 4.44. Free hydrochloric acid was not present in these mixtures.

Ninety-six infants, varying in age from 1 month to 3 years, were treated with this mixture. Of these, forty-seven had acute dyspepsia; nine, dysentery and twenty-one, parenteral infections; thirteen were on a mixed diet, and six showed spasmophilia. The mixture was given for a period of from seven days to three months. Infants over 9 months of age received additional food in the form of cereal, vegetables, etc.

The results were satisfactory in all cases. The infants took the mixture easily and showed good gains in weight. The spasmophilic infants did not receive medication, but all improved on this acid mixture.

THE ACTION OF PROTEINS, FATS AND CARBOHYDRATES ON THE NORMAL BLOOD SUGAR CURVE. B. L. STIRIKOVITSCH, Russian J. Pediat. **12**:117, 1928.

The normal blood sugar curve shows the reaction of the blood sugar to 25 Gm. of breast milk per kilogram of body weight. The milk is given by mouth. The author studied the blood sugar curves of infants (from 2 to 5 months of age) after adding a definite amount of either protein, sugar or fat to the breast milk. Twenty-five grams per kilogram of body weight, to which either 5 per cent of calcium caseinate (protein) 5 per cent of fat, or 5 per cent of sucrose or lactose had been added, was given to seven infants; the level of the blood sugar was then determined for a period of 150 minutes, at intervals of 15 minutes.

Briefly, the results were as follows:

1. There was a slowly rising blood sugar level following the intake of the breast milk with 5 per cent protein.

2. There was a quick but low rise in this level following the intake of milk with 5 per cent fat.

3. There was a quick and high rise in the blood sugar level following the intake of breast milk with 5 per cent of sugar.

4. The level reached after the first rise and fall of the blood sugar level was never below that following the intake of the milk with sugar; when protein was added, the fall was sudden and below the normal level.

5. The first rise of the blood sugar level lasted longest after the intake of the milk with the protein.

6. There were one or two more rises in the blood sugar level following the first fall, in the case of ingestion of the milk with sugar; the first rise, however, was the highest.

7. The second rise in the level of the blood sugar was higher than the first, in the case of ingestion of the milk with the protein.

8. There were a series of low secondary rises following the ingestion of the milk with sugar.

GASUL, Chicago.

Prenatal Conditions

BILATERAL HERNIA DIAPHRAGMATICA. DONALD PATTERSON, Proc. Roy. Soc. Med. **21**:1724; 1928.

A girl aged 7 years exhibited a swelling in the abdomen and a failure to thrive. An examination showed an undersized child. The liver was felt in the region of the right ilium but could be placed in the normal position. The entire chest was hyperresonant. Dulness was not present in the cardiac region. Feeding with bismuth showed the stomach to be bilocular with the upper portion above the diaphragm. When the child was inverted, the bismuth flowed into the upper sac. A few hours later the bismuth was seen in the small intestine which was lying in the right side of the chest. Roentgenograms are shown.

WILLIAMSON, New Orleans.

CONGENITAL CRANIOTABES. I. M. ARLUK, Nourrisson **16**:90 (March) 1928.

The author reviews enough literature to satisfy himself that the question of the relationship between congenital craniotabes and rickets is still open. The incidence of craniotabes is higher among infants of primiparous mothers. Both miscarriages and premature births augment its frequency. Ordinarily, craniotabes is not accompanied by defective ossification elsewhere in the skeleton. Pressure on the fetal head may be a partial factor though certainly a minor one. A constitutional anomaly is invoked in the absence of known etiology. In the cases analyzed, observations on blood chemistry are not cited.

MCCLELLAND, Cleveland.

HEMATOLOGIC INVESTIGATIONS IN PREMATURE INFANTS. OSKAR HERZ, Monatschr. f. Kinderh. **40**:1, 1928.

In a study of 103 premature infants, the writer found polycythemia in all of them during the first days. The hemoglobin count rose as high as 155 per cent in one case; the lowest recorded was 106 per cent. Erythrocytes varied from 4.5 to 7.5 million. The color index varied from 0.9 to 1.5. The white blood cell count was also inconstant, the cells ranging between 15,000 and 60,000. In many cases, granular cells took precedence over lymphocytes.

During the first few months in premature infants as well as in normal infants, there is a diminution in hemoglobin as well as in the number of red cells which decrease to less than 4 million. By the fifth month, however, signs of improvement are noted, and the condition again approaches normal.

Leukopenia and relative lymphocytosis are always associated with the anemia. This forms the triad of premature anemia.

The fact that the changes affect not only the red cells but the white cells and the fact that these changes are little influenced by any of the usual methods of treatment, such as the administration of iron and ultraviolet rays and injections of blood, leads the author to the conclusion that this anemia is not a physiologic

process. He is inclined to ascribe the whole condition to infections. To be an effective treatment, iron must be used in large doses, for example, ferrum reductum from 1 to 2 Gm. daily. Liver has a possible value, but ultraviolet rays have none. Irradiated ergosterol alone or in combination with liver, may have a beneficial effect but this is disputed. Irradiated ergosterol showed a marked effect on rickets, but its influence on the condition of the blood was uncertain. Occasionally, irradiated ergosterol and iron caused digestive disturbances.

GERSTLEY, Chicago.

A RARE COMBINATION OF MALFORMATIONS. N. M. NIKOLAJEW and J. S. DERGATSCHEW, Ztschr. f. Kinderh. **44**:406 (Oct.) 1927.

A girl, aged 4½ months, was born without extremities and at autopsy showed a long band extending from the posterior border of the spleen to the true pelvis where it united with the left ovary and the broad ligament. There was asymmetry of the skull and of the cerebral hemisphere. Follicles were not found in the spleen, and the islands of Langerhans were not present. This is the second case that has been reported in which malformation of the extremities and of the spleen was present.

EMERSON, Boston.

A CASE OF CONGENITAL ABSENCE OF THE THYROID GLAND. H. M. NICOLAEFF and E. B. CZIMBLER, Russian J. Pediat. **12**:38, 1928.

A case of congenital absence of the thyroid gland is described in an infant, aged 3 months and 2 days. The infant died of bronchopneumonia about one week after its entrance into the hospital. The article contains a report of a postmortem examination.

GASUL, Chicago.

Diseases of the New-Born

THE TREATMENT OF ASPHYXIA NEONATORUM BY THE INJECTION OF ALPHA LOBELINE INTO THE UMBILICAL VEIN. ROBERT S. WILSON, Am. J. Obst. & Gynec. **16**:379, 1928.

In a preliminary report, the author suggests the umbilical vein as a site of injection of alpha lobeline in persons with grave depression of the respiratory center. His results are striking, respirations starting in from seven to twenty seconds after injection. The suggestion is logical and should offer access for the injection of other substances used in resuscitation, such as epinephrine, without the dangers attendant on direct injection into the heart or longitudinal sinus.

ALLEN, Chicago.

VIABILITY OF THE NEWLY BORN. D. MACAGGI, Ann. de méd. lég. **8**:32, 1928.

In both civil and criminal legal procedures, the persistence of life after birth for even a few moments may be important. Questions of inheritance, survivorship and infanticide are intimately related to the manifestations of postnatal life and proofs that the child actually lived after birth. There are discriminations from both legal and purely biologic aspects, and there is a large literature in both law and medicine regarding these matters.

Observations are reported of strong and regular heart action continuing for two and one-half minutes after birth without respirations. From such apnea, asphyxia is said to differ by having weak and irregular heart beats. That problems of live or still birth are far from being simple is also illustrated by reports from some of the most competent pathologists of cases in which the lungs were devoid of air in the bodies of infants known to have cried out and lived as long as thirty hours after birth.

For a long time studies of these and closely related problems have been prosecuted at the Institute of Legal Medicine of the Royal University in Genoa under

the director, Perrando, and particularly of changes of the glands of internal secretion which may cause death soon after birth. In this report by Macaggi, at the twelfth Congress of Legal Medicine at Lyon in 1927, he adds several others to the description he made at a previous annual meeting, of airless lungs from newly born infants. He insists that the infants never breathed although they lived several hours, and regards the condition of the lungs as arrested development.

Many who have discussed this prolongation of life without apparent respiration have maintained that some exchange of gases actually does occur within the lungs. An opposing group to which Macaggi belongs attach great importance to the relatively large amount of hemoglobin possessed by new-born infants, the number of erythrocytes, the differences of respiratory exchange in the tissue and the many intrinsic conditions which favor persistence of life at the birth epoch. They also suggest that there may be a compensatory exchange of gases with oxygenation of hemoglobin in the stomach, bowel and skin.

Supporting such views are the evidences of maldevelopment of the lungs found in some of these infants; for example, lungs which have attained a development corresponding to only the fourth month of intra-uterine life found in the body of an infant living some hours after birth at the eighth month of gestation. Of course, Macaggi refers to careful histologic studies and to the care used in demonstrating the presence or absence of air in these lungs, to the importance of stains for elastic tissue, the Bielchowsky stain for reticulum and the amount and distribution of the elements of the pulmonary framework.

When attempts are made to promote breathing by artificial respiration, the infundibula or terminal intralobular bronchioles marking the utmost passages for air in such lungs are found ballooned out a little, with many hemorrhages caused by trying to get air into lungs which do not possess alveoli. The pulmonary lobules may be masses of tubules and diverticula lined with cylindrical epithelium and buried in an abundant stroma. Where there should be air sacs, there are masses of reticulum. That infanticide, or attempted infanticide, may be concerned with a child born alive and with lungs subsequently found airless by most careful examination, and still later by microscopic study found devoid of development proportionate to that of the rest of the body, is a matter of grave significance.

E. R. Le Count.

Acute Infections

The Rise in the Meningococcus Meningitis Rate. Public Health Rep. **43**:2519 (Sept. 28) 1928.

The reported incidence of meningococcus meningitis in the United States this year has already reached proportions that will make the 1928 rate higher than that of any year since 1918. In a group of twenty-eight states, the relatively low level of about two cases per 100,000 population in the four years prior to 1917 was followed by the high level existing during the period of the World War. For the next five years, the incidence of the disease apparently declined until it reached the prewar level. In 1926, there was some increase, which was followed by successively greater increases in 1927 and in 1928. The rate in the first half of the present year was much higher than that for the corresponding period in 1927 or 1926. This recrudescence has not yet appeared in other countries.

Sanford, Chicago.

Pertussis: Treatment with Ultraviolet Ray. W. W. McGaw, Texas State J. Med. **24**:224 (July) 1928.

During 1925 and 1926 201 children and 25 adults were treated with the Alpine lamp. The children, whose ages ranged from 3 months to 10 years, were stripped to the waist and both front and back were exposed to ultraviolet rays at a distance of 24 inches. In blonds under 2 years treatment was started with an exposure of fifteen seconds and the period of exposure increased by fifteen seconds

every other day, until it amounted to two and one-half minutes each for front and back. Initial exposure, for brunettes was one-half minute. In blondes over 2 years old, treatment was started at one minute and was increased one-half minute every second day until five minutes were reached. In brunettes treatment was started at one and one-half minutes. Blond adults received an initial treatment of two minutes and brunettes, three minutes; the period was increased one minute every second day.

Relief from vomiting, whoop and paroxysmal cough was noted in 52 per cent of the children; 38 per cent improved, although the paroxysmal cough continued. Ten per cent were unchanged. Of twenty-five adults, 80 per cent were cured and 20 per cent improved.

Improvement was evident after the second and third treatment; the duration of the disease was shortened two or three weeks in half of the cases. The 10 per cent who were not improved did not receive a sufficient number of treatments.

Increased appetite and gain in weight were found in 90 per cent of this series.

MOORE, Dallas.

SCARLET FEVER: RICINOLEATED ANTIGEN IN THE PREVENTION. EDWARD J. CAMPBELL, Wisconsin M. J. **27**:411 (Sept.) 1928.

The first step in epidemic control is to prevent the spread of the disease within the quarantined home. The use of scarlet fever antitoxin was discontinued during this study because of severe reactions and the short duration of immunity conferred. Dick's toxin also caused severe reactions. Eight pupils out of 450 receiving ricinoleated scarlet fever antigen during an epidemic developed mild scarlet fever in from 8 to 180 days. The control group had a higher incidence of reaction and more severe illness.

JANNEY, Milwaukee.

A CASE OF GANGRENOUS CHICKENPOX DUE TO B. DIPHTHERIAE. ALEXANDER ZOE, Brit. J. Child. Dis. **25**:111 (April-June) 1928.

A boy, aged 13 weeks, was admitted with the typical lesions of chickenpox. Eleven days after admission several of the lesions showed an angry areola, and sloughing occurred. Ten days later, a blood-stained nasal discharge showed *B. diphtheriae* on culture. Two thousand units of diphtheria antitoxin were given. Profound toxemia set in, and the child died. Cultures from the lesions in the skin showed *B. diphtheriae*.

LANGMANN, New York.

PROPHYLAXIS FOR DIPHTHERIA. G. LAPIERRE, l'Union méd. du Canada **57**:574 (Oct.) 1928.

The author concludes that vaccination against diphtheria establishes immunity in a period of from six to seven months. It gives an absolute immunity and should be done preferably at the end of the first year. The method adopted consisted of a first injection of 0.5 cc., in the fall, followed by a second injection in four weeks. Six months later, a third injection of 0.5 cc. was given, followed in four weeks by one of 1 cc.

THE FREQUENCY OF NASAL DIPHTHERIA IN CHILDREN. P. LETONDAL, l'Union méd. du Canada **57**:584 (Oct.) 1928.

During the past winter, the author systemically searched for the diphtheria bacillus in the nose of all infants up to 30 months of age admitted to his service, who suffered from infections of the upper portion of the respiratory tract. In 100 cases, he was able to find only one case of nasal diphtheria, which led to the conclusion that nasal diphtheria in young children was not as common as usually believed.

SANFORD, Chicago.

ABERRANT TYPHOID INFECTIONS. R. TURQUETY and SUZANNE DREYFUS, Nourrisson **16**:228 (July) 1928.

The reader is reminded that *B. typhosus* may wander far in the human body and give rise to a number of widely separated and unrelated acute infections, such as cholecystitis, meningitis, pleurisy and arthritis. These extra-intestinal infections may be complications of enteric fever or may occur without it. A case is described in a girl, aged 6 years, who developed severe bronchopneumonia. An intestinal hemorrhage occurred on the eleventh day. The stools were examined for typhoid bacilli at this time but none were found; the Widal reaction was negative. Signs pointing to lesions of the central nervous system supervened, but the cerebrospinal fluid gave a negative reaction. Finally, a lung puncture was done; *B. paratyphosus* A was recovered in the cultures. At this time, a positive Widal reaction, 1:50, was obtained for the paratyphoid A bacillus. The child died on the twenty-fourth day of illness. The authors report this as a case of true paratyphoid bronchopneumonia. They were unable to find a report of a similar case in the literature.

McCLELLAND, Cleveland.

THE CARDIAC SYMPTOMS IN SCARLET FEVER. F. REINHARD, Arch. f. Kinderh. **84**:210 (June 15) 1928.

Eighty-four of 160 children suffering from scarlet fever were found to have the so-called "scarlet fever heart." The heart sound is characteristic: The murmur is hardly loud enough to be called such; the term "impurity" might be more suitable. This sound exists as a soft systolic noise over the apex. A splitting of the second sound, usually the second pulmonic beat, is often noted. Subjective symptoms usually are not present, although the pulse is irregular, and the left portion of the heart is frequently enlarged. Nineteen of the children presented the symptoms on the second or third day of the illness. In thirty-six, the symptoms appeared between the fifth and twenty-first days, in four in the fifth week, and in two in the sixth week. In only ten children did the symptoms clear up in two or three weeks, and in twenty-four they had disappeared entirely in six weeks. Sixty children left the hospital with cardiac symptoms. Thirty-five of these children were under observation after discharge; the symptoms of heart disease disappeared in thirteen in four months, and in eleven there was improvement. Three children were examined nine months after their illness, and the murmur was still present. This condition of the heart is not dependent on the severity of the scarlet fever nor is it connected with rheumatism or nephritis. It is probably a degenerative process of the myocardium. Treatment is not needed, as a spontaneous recovery appears to be the rule.

A CASE OF MEASLES WITHOUT EXANTHEM. H. KOEPPE, Arch. f. Kinderh. **84**:226 (June 15) 1928.

A child, aged 18 months, developed a slight coryza with a temperature of 38.3 C. (100.9 F.) eleven days after exposure to measles. The fever reached 38.7 C. (101.6 F.), its peak, three days later. No cause could be found. The ears were normal, and Koplik's spots were not present. On the fourth day, the tonsils were slightly reddened; on the fifth, the urine contained a trace of albumin and a few cells. A Pirquet test which gave a positive reaction before the fever was negative when made on the seventh day. The next day the Mantoux test was positive. The fever curve resembled measles, but the general condition of the child was excellent. Fourteen days after the appearance of fever, another child who had been with her at the time developed a measles exanthem. This child could not have contracted the disease in any way except through contact with the child previously described. Two years later the same child, with two other children, was exposed to measles in the clinic. They contracted the infection while she did not.

SANFORD, Chicago.

MEASLES ATTENUATED BY THE USE OF SERUM. H. ALSCHWANG, Monatschr. f. Kinderh. **39**:101, 1928.

In an epidemic in the writer's institution convalescent serum, given from three to four weeks before the onset, and mothers' serum, given in the first days of the incubation period, seemed to cause an attenuated form of measles with fewer complications.

ORAL ADMINISTRATION OF DIPHTHERIA TOXIN-ANTITOXIN. HANS BISCHOFF, Monatschr. f. Kinderh. **39**:305, 1928.

From results obtained by the Schick test, the author concluded that the oral administration of the toxin-antitoxin mixture was valueless in immunization against diphtheria.

INCIDENTAL EFFECTS OF INJECTIONS OF DIPHTHERIA ANTITOXIN. CHEN HUNG-TA, Monatschr. f. Kinderh. **39**:482, 1928.

A number of purified serums were studied to determine whether there was less sickness following the injection of a particular serum. The experiment was concerned principally with the Bram serum. The author did not find the Bram serum in any way superior to the other varieties of serums.

GERSTLEY, Chicago.

THE TREATMENT OF PERSONS WITH SCARLET FEVER WITH BEHRING SERUM. E. GOTTSCHE, München. med. Wchnschr. **75**:1455, 1928.

The author has used the Behring serum a number of years and reported the results. His present group comprises 622 cases divided in five groups. Fifty per cent go in the first group, in which the temperature returned to normal in from twelve to twenty-four hours with no deaths or complications. Of the patients in the other groups having complications, the untreated did about as well as the treated, except that the complications were less severe in those treated. The author's belief is that the Behring scarlet fever antiserum is as important in treatment as is diphtheria antitoxin in diphtheria.

SCHORER, Kansas City, Mo.

THE PATHOLOGY OF PERTUSSIS. GOLDMAN, Ztschr. f. Hals-, Nasen- u. Ohrenh. **18**:590, 1927. (From the Proceedings of the German Otolaryngologic Congress.)

As the result of careful investigation of a number of cases during an epidemic, the author believes that paranasal sinuses, especially the antrums and ethmoids, are the principal seat of infection. He calls attention to the symptomatology — first serous, later mucoid, nasal discharge. He believes that this dense glutinous discharge flowing down the nasopharynx starts the cough. The whoop, he thinks, is due to spasmodic contraction of the glottis following maximal pumping out of the air of the thorax by the prolonged cough, which brings about marked negative intrathoracic pressure, causing a powerful inspiration, and also aspiration of secretion, which secondarily infects the bronchi.

He says further that chronic paranasal sinus disease is the cause of the recurrence of pertussis.

He advises as treatment during the acute stage, rest in bed, diaphoresis, inhalations, suction and heliotherapy and heat for the head; later, irrigation of the affected sinuses, especially in stubborn cases.

LEWY.

FACIAL DIPLEGIA IN POLYNEURITIS OF A DIPHTHERIA CARRIER. PETER KÖNIG, Ztschr. f. d. ges. Neurol. u. Psychiat. **114**:200 (April) 1928.

König reports a case of polyneuritis in a woman, aged 48, with a sudden onset of paraplegia, pains and paresthesia in the legs, and mild pareses in the fingers;

the next night after the onset there was a bilateral facial paralysis. This was of peripheral type with electric reactions of degeneration. Cultures of diphtheria bacilli were obtained from the pharynx and tonsils. After two injections of serum, all the symptoms disappeared. König reports the case because the occurrence of polyneuritis in a carrier is unique and because facial diplegia in diphtheria is rare.

ALPERS, Philadelphia.

SENSITIVENESS TO EPINEPHRINE IN CHILDREN WITH SCARLET FEVER. A. KROVITZKY and A. ORLOVA, Ztschr. f. Kinderh. **45**:635 (June) 1928.

The degree of sensitiveness to epinephrine reveals the functional condition of the vegetative nervous system in cases of scarlet fever. In the first period of the disease (one to five days) sensitiveness to epinephrine is increased; in the second period (five to twenty days) it is greatly diminished, and in the third period (after the twentieth day) the vegetative nervous system, in uncomplicated cases, comes into equilibrium. According to Lenart and Sandor, the increase in sensitiveness to epinephrine during the first days of the disease and in healthy children showing a positive reaction to the Dick tests indicates that the great majority of vagotonic children are disposed to scarlet fever.

SPONTANEOUS IMMUNIZATION AGAINST DIPHTHERIA IN INMATES OF INSTITUTIONS. J. ROSENSTERN, Ztschr. f. Kinderh. **45**:640 (June) 1928.

Rosenstern found that a slight diminution in the number of carriers of diphtheria and a decrease in the number of infections with diphtheria occurred with lengthened stay in the institution, without an increase in the number of negative reactions to the Schick test among children and without any self-immunization by silent infections. It may be that intensive treatment with fresh air, both day and night, throughout the year and sunlight brings about this self-purification.

THE MEANING OF CYLINDROIDS IN THE URINARY SEDIMENT IN THE PATHOLOGIC STUDY OF NEPHRITIS FOLLOWING SCARLET FEVER. F. L. SPANIR, Ztschr. f. Kinderh. **45**:729 (June) 1928.

The occurrence of single precylinders, that is, cylindroids, does not have any clinical significance. The demonstration of them in the urinary sediment in great quantity, however, points to an abnormal circulation of blood in the tubules of the kidney and in acute infectious diseases indicates a possible preexisting complication with nephritis or nephrosis. The reappearance of precylinders in the convalescent stage of nephritis or nephrosis may be considered a favorable sign.

EMERSON, Boston.

VACCINATION AGAINST CHICKENPOX. G. PETENYI, Orvosi hetil. **72**:115, 1928.

Different methods of active immunization were used in a number of cases. In twenty-five cases, the controlling of the immunity was satisfactory. In sixteen of these there was acquired immunity. In five it lasted from 40 to 45 days and in eleven, from 60 to 200 days. As material for immunization, blood in amounts of from 0.1 to 1 cc. or from 0.005 to 0.01 cc. of the content of vesicles can be used subcutaneously. Killed virus, the content of vesicles, blood serum, or cerebrospinal fluid can be used for active immunization. In some of the cases, a mild form of chickenpox developed, characterized by a rudimentary form of eruption lacking the usual polymorphism of the vesicles.

ZENTAY, St. Louis.

ACTIVE IMMUNIZATION AGAINST MEASLES. G. PETENYI, Orvosi hetil. **72**:148, 1928.

The author's experiments with active immunization against measles were independent of similar work done by Japanese and French authors. He produced a milder form of measles by injecting from 1 to 3 cc. of blood taken from a patient

during the first twenty-four to thirty-six hours of the exanthematous stage. On the whole, the picture was similar to that of the so-called abortive measles. The temperature was lower and of shorter duration. The catarrhal manifestations were most marked in the mouth. Koplik spots were always present, their number being independent of the rest of the clinical picture. The rash was milder than that of abortive measles, and the spots were smaller and less dense. The exanthematous stage was not typical of measles and a diagnosis of measles without information as to inoculation would hardly have been possible. The incubation period was somewhat shorter. Untoward effects were not seen. The method may be used in hospitals when convalescent serum is not easily available.

PREDISPOSITION TO SCARLET FEVER AND AUTONOMOUS NERVOUS SYSTEM. G. LENART and KLARA SANDOR, Orvosi hetil. **72**:319, 1928.

The authors examined the autonomous nervous system by intravenous injections of epinephrine and compared its relationship with positive or negative reactions to the Dick test. The results showed that children with a positive Dick reaction have an increased sensitivity to epinephrine and those with a negative reaction showed a decreased sensitivity. This would prove that in children giving a negative reaction to the Dick test, the vagotonic constitution would be characteristic, whereas in those reacting positively, sympathicotonia would more often be found.

THE EFFECT OF INTRAVENOUS AND ORAL ADMINISTRATION OF SODIUM BICARBONATE ON SPASMS IN TETANUS. P. HEIM, Orvosi hetil. **72**:407, 1928.

The spasms in the muscles in tetanus are caused by the effect of toxin on the motor ganglion cells of the spinal cord. It is probable, however, that the lactic acid produced in the muscles may contribute toward the production of long continued spasms. The intravenous injection of from 30 to 40 cc. of a 10 per cent solution of sodium bicarbonate had a beneficial effect on the spasms. The good effect did not last longer than from three to five hours, but repeated injections of sodium bicarbonate brought relief again. This method of treatment together with the usual antitoxic treatment seems to be of value in the treatment for tetanus.

HEMOLYTIC STREPTOCOCCUS IN SCARLET FEVER IN CONVALESCENTS AND IN HEALTHY PERSONS. B. KANYÓ, Orvosi hetil. **72**:747, 1928.

In recent cases of scarlet fever, large numbers of hemolytic streptococci can be found in the throat. In convalescents, the symptoms are less constant, but even after a period of six weeks, they are positive in 38 per cent of the cases. Hemolytic streptococci may be found in the throats in about 9 per cent of normal persons. These carriers of hemolytic streptococci usually give a negative reaction to the Dick test. The results show the importance of hemolytic streptococci in the etiology of scarlet fever. It appears desirable that the excretions from the throat should be examined bacteriologically as is usually done in diphtheria before the patient leaves the hospital. If hemolytic streptococci are found in the throat in these cases and also in cases showing complications, such as acute otitis media, isolation for six weeks is not sufficient.

In the wards for patients with scarlet fever, the convalescents should be isolated from the new patients, and the mouth and throat should receive careful attention.

ZENTAY, St. Louis.

SEVERE FORMS OF SCARLET FEVER. F. E. EDELMAN, Russian J. Pediat. **12**:14, 1928.

The author differentiates between three types of the severe form of scarlet fever: the toxic, the septic and the mixed.

The toxic type affects chiefly the sympathetic nervous system. It is characterized by high fever, severe vomiting, great restlessness, amounting in some

cases to delirium, and coma. The involvement of the endocrine vegetative system is revealed by the following observations: absence of white dermographism, low blood pressure, rapid pulse, arrhythmia, contracted pupils, enlargement of the conjunctival vessels, the paradoxic reaction to injections of epinephrine and the negative reaction to cocaine (2 per cent). Pathologic examination revealed degeneration of practically all the ganglion cells of the sympathetic nerves. The author studied twenty-three cases of the toxic type; thirteen of these patients died and eleven recovered. All of those who recovered received Moser's serum. (The author did not use Dick's serum.)

Of 49 patients with the septic type of the disease, 37 died. Among 54 persons with the mixed type, there were 34 deaths. Endocarditis and myocarditis were the rarest complications, occurring in only 2 of 120 cases.

The toxic type showed the smallest mortality rate. The use of Moser's serum is highly recommended, especially in the toxic type. The serum does not appear to be of great value in the septic and mixed types of scarlet fever.

So-Called Scarlet Fever Croup. B. H. Kartashawa, Russian J. Pediat. **12**:30, 1928.

The fibrinous inflammation of the larynx and trachea by the same organism that causes scarlet fever is declared to be rare. Among 571 autopsies performed on patients who had died of scarlet fever, only 8 revealed a streptococcic laryngotracheitis. This form of croup should be differentiated from diphtheritic laryngitis.

Gasul, Chicago.

Chronic Infections

Tuberculous Infection of the Lungs in Early Infancy: Report of a Case Observed from Twelve Weeks to Over Five Years of Age. Jerome L. Kohn, Am. Rev. Tuberc. **18**:565 (June) 1928.

A well developed breast-fed infant, during the ninth week of life, developed noisy breathing with inspiratory and expiratory dyspnea which continued over a period of several weeks. The temperature was normal except during the first day in the hospital, when it was 103 F. A roentgenogram showed atelectasis of the right upper lobe, emphysema of the right lower lobe, and displacement of the heart and mediastinum to the left. The Pirquet test was positive at the twelfth week of life. Bronchoscopic examination showed the right main bronchus narrowed to a crescentic slit, probably due to external pressure. These signs and symptoms continued, with intermissions, over a period of three months. During all of this time, the child was afebrile, except on the one occasion mentioned, and gained in weight. He was observed over a period of five years, and progressed normally. He had few infections of the upper respiratory tract but had pertussis during the year before admission to the hospital, from which he completely recovered. The Pirquet test remained moderately positive. The primary focus was first demonstrated in the roentgenogram when the child was 3 years and 2 months old. When he was 5 years of age, it was calcified and more compact. Adenopathy of the right hilum was first seen when the child was 21½ weeks of age; and some infiltration of the right lower lobe was noted at the age of 7½ months. At the time the paper was written, the lung fields were clear, but shadows at the right hilum were more dense than the left. The source of the infection was never definitely ascertained.

The Pathology of Pulmonary and Bronchial Gland Tuberculous in Infancy and Childhood. P. F. Armand-Delille and C. Lestocquoy, Tubercle **9**:359 (May) 1928.

The authors studied the progress of tuberculous infection in young subjects by means of serial x-ray examinations, commencing at the earliest possible stage of the disease and comparing the results of such examinations with subsequent

observations at autopsy. A special technic was used in the postmortem examinations in order to preserve the normal relationships of organs and glands. The thoracic contents were removed in one mass and hardened in casts which were the size and contour of the chest of a child of corresponding age. On the basis of these studies, the authors draw the following conclusions:

Tuberculous bronchial glands are always enlarged, but when they occupy the middle of the mediastinum, they can rarely be observed by x-ray examination, since they are usually masked by shadows of the heart and vessels. So-called "perihilar" shadows are not due to glands, since the latter can give rise only to juxtatracheal shadows. The primary lesion, almost always demonstrable on careful postmortem examination, is rarely shown on the x-ray plate. It is frequently localized in the pulmonary base, obscured by shadows of the heart, liver, stomach or spleen. Good x-ray plates may reveal the presence of miliary tuberculosis early in the course of the disease. Lobar shadows which persist for months may be due to other than tuberculous disease, and diagnosis on the basis of x-ray examination alone may be exceedingly difficult. When, however, these shadows are seen progressively to invade other lobes or cross over to the opposite one, prompt collapse therapy by artificial pneumothorax is indicated.

Tuberculosis is best controlled in childhood by efficient medicosocial work. The Calmette vaccination and the removal of children from contact have been most successful. Following the adoption of these measures in 3,500 children of Paris under the supervision of the authors, morbidity has fallen from 60 to 0.2 per cent, and mortality from 40 to 0.06 per cent.

SMITH, Ogden, Utah.

SEDIMENTATION TEST IN CONGENITAL SYPHILIS. SOPHIE WEISS, Nourrisson **16**:102 (March) 1928.

Three hundred and eighty examinations were made on 180 infants varying in age from 3 weeks to 5½ years. Among these were 140 cases of congenital syphilis. The V. S. (vitesse de sedimentation) was determined from one to fifteen times in each infant. The following conclusions were reached:

Congenital syphilis causes an acceleration in the sedimentation of the red blood cells. This acceleration parallels the severity of the disease in cases showing visceral and osseous involvement and is least marked in cases exhibiting only slight cutaneous lesions. Improvement following antisyphilitic treatment is accompanied by a retardation of the reaction. Infants of syphilitic mothers, who have undergone energetic treatment during pregnancy, have a normal sedimentation time.

The author feels that the test is of real value especially in recognizing latent cases. Both the simplicity of the technic and the cheapness of equipment required recommend it.

PARROT'S PARALYSIS WITH SUPPURATIVE ARTHRITIS. R. BROCA and R. DEMAILLY, Nourrisson **6**:218 (July) 1928.

The pseudoparalysis described by Parrot in 1872 is caused by a syphilitic osteochondritis of such severity that movements of the affected arm or leg are painful; less extensive lesions may occur but can be discovered only by roentgenograms. The osteochondritis is sometimes accompanied by a true syphilitic arthritis. In such cases, it is necessary to determine the nature of the arthritis. An exploratory puncture should be made, and the material obtained should undergo a bacteriologic examination. In patients with syphilitic arthritis, the pus contains polymorphonuclear leukocytes, but no micro-organisms are found either in direct smears or in the cultures. X-ray examination gives useful information as to the character of the osteochondritis. Other helps in differential diagnosis are the presence of a positive Wassermann reaction and the absence of fever and local signs of acute inflammation. The authors believe that this is a frequent complication of Parrot's paralysis. The shoulder joint is the one most frequently involved; polyarthritis has not been observed. Patients suspected of having the disease should always be

given the benefit of antisyphilitic therapy, as the response in the specific cases is prompt and the prognosis favorable. The condition usually appears during the first three months of life, although a few cases in later infancy are reported.

McCLELLAND, Cleveland.

THE TREATMENT OF TUBERCULOSIS BY METHYLATED ANTIGEN. CAMINO, Rev. de la tuberc. **9**:211 (April) 1928.

Observation of forty-two patients with various forms of tuberculosis who were treated with methylated antigen led Camino to conclude that of all laboratory products, this agent gives the best results with the least risk. Its function, however, is that of an adjuvant to such proved measures as rest, hygiene, diet, climate and collapse therapy. With careful technic and graduation of doses, harmful reactions are easily avoided. An elevation of temperature sometimes occurs, especially in patients who are already febrile. Local reactions, pleurisy and hemoptysis have occurred following its use but not to such a degree as to require cessation of treatment. The most evident results following its use are the improved condition of the patient and an increase in appetite, strength and weight. Expectoration often becomes less purulent, or may disappear entirely. The temperature becomes lower and tends to grow stabilized. Pleural effusion following pneumothorax is favorably influenced.

With careful supervision, ambulatory patients as well as those in the sanatorium may be given the benefit of this treatment.

SMITH, Ogden, Utah.

SYPHILIS OF THE RESPIRATORY TRACT IN CHILDREN. J. C. NAVARRO and E. A. BERETERVIDE, Semana méd. **2**:471, 1927.

This rare form of syphilis is classified into: first, laryngopharyngeal; second, bronchial, which is further divided into acute, subacute prolonged and chronic or bronchiectatic; third, pulmonary, divided into hemoptic, infiltrative and pseudotubercular.

Four cases are presented of the laryngeal form, which resembles a form of pseudocroup with attacks of stridor and dyspnea. This group did not present any other signs of syphilis or fever. An examination of the exudate from the larynx disclosed the spirochetes. The Wassermann test gave a decidedly positive reaction in all cases.

Two cases were reported of the acute bronchial form which is characterized by an acute onset with fever, cough and rapid respiration. The lungs were full of râles, and the spleen was enlarged. These cases reacted favorably to specific treatment.

Nine cases were reported of subacute or prolonged bronchitis which is characterized by an inability of the symptoms to subside in the usual time. The roentgenograms showed moderate infiltration. Signs of syphilis were otherwise present, and all cases responded to specific treatment.

Eight cases of bronchiectasis in older children were presented. These were characterized by profuse purulent expectoration. The roentgenograms showed moderate infiltration as if from a tuberculous process. All the cases responded to specific treatment.

The hemoptic form was found in three cases which showed the symptoms of a continued and profuse bloody expectoration. The roentgenograms of this group showed infiltration. These cases failed to disclose the Koch bacillus, and all responded to antisyphilitic treatment.

There were four cases of the infiltrative form which is of two types: the gummas, which are at first inflammatory with catarrhal symptoms and later sclerotic, and the syphilitic pneumonias. The roentgenograms in these cases distinctly showed dense infiltration or areas of pneumonia. Recovery followed specific treatment.

Two cases, both in older children, displayed the semituberculous form in which the lesions take on a tuberculous character with the formation of a definite cavity.

The symptoms were quite like those of tuberculosis, with loss of weight and a low grade temperature. Examination disclosed the cavity which was confirmed by roentgenograms. Hemoptysis was marked. Koch bacilli were not found and both patients recovered with specific treatment.

All of the foregoing cases are excellently presented with full notes of progress and with roentgenograms. An excellent bibliography of these rare conditions is given.

THE ORGANIZATION OF A CHILDREN'S TUBERCULOSIS CLINIC. J. DUKEN, Arch. f. Kinderh. **84**:81 (May 25) 1928.

Duken tells of the problems encountered in the organization of the Children's Tuberculosis Clinic in Jena in 1923. Great discrepancies were found in the number of children reported for treatment. One school, for example, reported 60 per cent of its scholars in need of treatment, while another school reported none. The children were from every social stratum, and the pathologic changes found were varied. One school reported that 18 per cent of its children had defective spinal curvature. Another reported the diagnosis in children aged 13 and 14 years as follows: 25 per cent had heart disease, 30 per cent scrofula, 25 per cent anemia and 33 per cent rickets.

THE PROGNOSIS OF TUBERCULOSIS IN THE FIRST YEAR OF LIFE. D. BAUMLER, Arch. f. Kinderh. **84**:136 (May 25) 1928.

In 154 cases of tuberculosis in children less than 2 years of age, the mortality was as follows: under 6 months, 50 per cent; 7 to 12 months, 29 per cent, and 13 to 24 months, 20.4 per cent. The majority of these cases gave a positive tuberculin reaction. Twenty cases, among children less than 6 months old, showed all the lesions to be in the lungs. In thirty-four cases, among children aged from 6 months to 1 year, two lesions were in the peritoneum and the remainder in the lungs. In fifty-eight cases, among children aged from 13 to 24 months, one lesion was in the peritoneum, four were in the cervical glands, one in the mesentery, and the remainder in the lungs.

PRIMARY TUBERCULOSIS IN A LESION OF THE LIP. J. DUKEN, Arch. f. Kinderh. **84**:223 (June 15) 1928.

A child, aged 2 years, had a small ulcer with a grayish-white coating on the upper lip. It resembled an impetigo lesion but did not have a tendency to form a crust. It was the only lesion found on the body and had been present for about two months. Tuberculosis was not present in the family, but the child had been in close association with an adult with pulmonary tuberculosis who had been recently discharged from a hospital for tuberculous patients. The lesion did not respond to treatment for impetigo, and the cervical glands became enlarged. On incision, a creamy pus was discharged. The glands healed poorly, and fistulas remained for several months. The tuberculin test was not applied until four months after the initial symptoms. It was then highly positive, and the child was sent to a clinic. All roentgenograms were negative, and signs of tuberculosis could not be found elsewhere. Ultraviolet irradiation and a balanced diet were then given; in two weeks the ulcer was transformed to a bluish scar. Duken believes that the course of the disease indicated primary tuberculosis.

SANFORD, Chicago.

CONGENITAL SYPHILIS AND FEEBLEMINDEDNESS IN CHILDHOOD. G. STELLER, Monatschr. f. Kinderh. **40**:42, 1928.

A comprehensive review of the literature is supplemented with certain observations of the author. The article should interest a neurologist more than a pediatrician. Apparently, much work remains to be done before definite conclusions can be reached.

QUANTITATIVE INVESTIGATIONS INTO TUBERCULIN SENSITIVITY ESPECIALLY IN SCROFULA. ERNST HARMSTORF, Monatschr. f. Kinderh. **40**:270, 1928.

By quantitative methods, the author demonstrated that susceptibility to tuberculin did not differ between children with ordinary forms of tuberculosis and those with scrofula. The skin of scrofulous children, however, showed a greater susceptibility to general irritants.

GERSTLEY, Chicago.

Internal Diseases

POSTMORTEM FINDINGS IN ACUTE JELLY-FISH POISONING WITH SUDDEN DEATH IN STATUS LYMPHATICUS. H. W. WADE, Am. J. Trop. Med. **8**:233, 1928.

An autopsy is reported of a case of acute poisoning from a jelly-fish with sudden death. The patient was a well developed young man of status lymphaticus type, with slight residual evidences of epilepsy. Besides the local injury at the site of contact with the tentacles of the jelly-fish, there were pulmonary edema, engorgement of the right side of the heart, congested viscera and evidence of injury to the parenchyma of the kidney.

PEARL ZEEK.

STUDIES IN ASTHMA: THE USE OF VACCINES IN ASTHMA AND IN COLDS. FRANCES M. RACKEMANN and MARGARET A. SCULLY, New England J. Med. **199**:314 (Aug. 16) 1928.

This series of cases from the Anaphylaxis Clinic of the Massachusetts General Hospital includes forty-nine which have been followed for several years. Treatment has been carried out in fairly definite courses, for three years or more in most of them with new courses of vaccine each fall and winter.

Twenty-three of the forty-nine patients were treated from year to year with the same type of bacteriologic vaccine, whether stock or autogenous, while the other twenty-six received different types of vaccine in each course of treatment.

In all of the 39 children among the 346 patients with asthma, the results were good.

The conclusions reached concerning the results and the mechanism of vaccines in asthma and in "colds" are essentially the same. With the technic described, 346 patients with asthma have been treated with vaccines, in 74 per cent with good results. In the prevention of "colds," vaccines have been given to a series of 101 patients, in 68 per cent with good results. Both in asthma and in colds, these results are usually only temporary, but since they can be reproduced by repetition of the treatment, they are important. Both in asthma and in colds, the results for the whole series indicate that stock vaccines are just as effective as autogenous vaccines; this fact shows that the effect of vaccines is nonspecific.

A closer study of the patients treated from year to year shows that repeated courses of treatment with the same kind of vaccine leads to the same result. Treatment of the same patient in different courses with different vaccines yields, at times, similar results, indicating a nonspecific effect of vaccine. Often, however, the results are dissimilar, one vaccine working better than another; this fact seems to indicate a degree of specificity in the action of the vaccine.

Considering the cases as a whole, one organism cannot be proved more important than another in the treatment for either asthma or colds.

It is suggested that the good effects of vaccine depend on an unknown reaction which takes place when a particular vaccine is injected into a particular patient. Evidently the production of such a reaction depends on conditions which are to some extent restricted, and to this extent the treatment would appear to be specific. Whatever the mechanism, it is the same in asthmatic as in nonasthmatic persons.

GENGENBACH, Denver.

INVESTIGATIONS ON THE PIRQUET AND WASSERMANN REACTIONS IN ASTHMATIC CHILDREN. KAJ H. BAAGÖE, Brit. J. Child. Dis. **25**:107 (April-June) 1928.

A positive Pirquet reaction did not occur more frequently in children with asthma than in children without active tuberculosis. Syphilis, as determined by the Wassermann reaction, was not found to affect the development of asthma.

TREATMENT OF CHRONIC POLYMICROBIAN COLITIS IN CHILDREN. A. P. CAWADIAS, Brit. J. Child. Dis. **25**:161 (July-Sept.) 1928.

The author bases his views chiefly on experience gained in the Evangelismos Hospital in Athens. He considers that most cases of intestinal inflammation are due to a combination of exo-infection and auto-infection. The two great classes of colitis from auto-infection are colitis caused by saccharolytic auto-infection and colitis caused by proteolytic auto-infection.

Dietotherapy, oral vaccinotherapy, adsorption and astringent therapy and bacteriotherapeutic preparations are mentioned, as well as sunlight treatment with spas and psychotherapy.

CASE OF SPLENECTOMY FOR PURPURA HAEMORRHAGICA. HAZEL H. CHODAK GREGORY, Brit. J. Child. Dis. **25**:180 (July-Sept.) 1928.

For two years, a boy, aged 7 years, had hemorrhages from the nose and into the skin on several occasions. The bleeding time was fifteen minutes, and the coagulation time was normal; the clot was nonretractile, and the platelets numbered 47,700. Splenectomy was done, dense adhesions being found between the spleen and the anterior abdominal wall and also between the omentum and the anterior abdominal wall. In fifty recorded cases, a considerable number showed perisplenitis. A year after the operation, the boy's general health was reported greatly improved and except for two slight nosebleeds he had been free from hemorrhages.

LANGMANN, New York.

STATUS LYMPHATICUS AND SUDDEN DEATH. J. ANDERSON and J. A. M. CAMERON, Glasgow M. J. **108**:129, 1927.

This report is based on 100 cases in which a study of the gross disease was made in all the bodies, and of that histologically demonstrable in fifty. It is not stated over how long a period the observations extended. This is of considerable interest since thirty of the bodies were of children under 18 months of age who died when anesthetized for less than ten minutes with chloroform. The weight of the thymus, from 8 to 10 Gm., regarded as normal in Glasgow for the age of 2 years, is probably less than has been found normal in other places. Some disease was frequently present in the thyroid gland and in the suprarenal glands, and the chromaffin cells of the medulla were fewer than normal.

Importance is attached to these changes, but still more to disseminated fatty degeneration in the intima of arteries of all sizes. Illustrating the significance of this disease, mention is made of death of two adults, aged 21 and 23 years respectively, from intracerebral hemorrhage and status lymphaticus with widespread fatty intimal arterial degeneration. In a third person, aged 16 years, some of the arteries involved served the nodes and muscles of the His bundle system in the heart, and there was paroxysmal tachycardia, with hemorrhages in the myocardium in addition to the systemic hyperplasia of the lymphoid tissue. The article is a valuable addition to the literature of this subject because of new evidence offered for the recognition of status lymphaticus and new suggestions to explain its mortality. Allusion is made to the possibility of a deficiency of epinephrine and the hypoglycemia which presumably would follow.

E. R. LE COUNT.

A Case of Paltauf-Sternberg Disease (Malignant Lymphogranulomatosis). Nobecourt, Med. de los ninos **29**:111 (April-May) 1928.

A boy, aged 14 years, developed malaise and fatigue; a few weeks later a mass appeared in the supraclavicular region. Radiographic examination revealed a large tumor in the anterior superior mediastinum. Biopsy showed the enlargement in the neck to be a lymph gland, which on section was white and dense. In its center a homogeneous sclerosis was found, with many lymphocytes, neutrophils, some eosinophils and numerous cells of Sternberg. These are large multinuclear cells, with clear cytoplasm; at times many show mitosis. Sternberg first described the lesion as an atypical form of tuberculosis of the lymphatic system, but later regarded these cells as evidence of a true neoplasm.

Examination of the blood revealed: 2,500,000 erythrocytes; 14,000 leukocytes; hemoglobin, 55; neutrophils, 79 per cent; eosinophils, 2 per cent; large mononuclear leukocytes, 6 per cent; small mononuclear leukocytes, 9 per cent; lymphocytes, 2 per cent, and transitionals, 1 per cent. There were no abnormal red or white blood cells. Bleeding and coagulation occurred normally. The Wassermann reaction was negative and the tuberculin test positive.

The patient first developed a high pitched voice, then suffered loss of voice which attributed to pressure on the nerve in the mediastinum. He vomited from time to time, rapidly lost weight and died three months after the condition was diagnosed. A leukopenia developed with a persistent polynucleosis (80 per cent).

Pathologic Conditions of the Lungs and Their Diagnosis. J. Duken, Arch. f. Kinderh. **84**:108 (May 25) 1928.

For the last three years Duken has used the method of contrast filling of the bronchi. Interesting cyst formations, the presence of which was entirely unsuspected, were frequently found by this method in the lungs. A mongolian idiot, aged 4½ months, had an unsuspected degenerative cyst in the left apex of the lung. A child, aged 8 years, had an unsuspected fetal bronchiectasis, and one of 13 years, congenital bronchiectasis.

Expiratory Gasping and High Pitched Cough Caused by a Foreign Body in the Esophagus. J. Duken, Arch. f. Kinderh. **84**:120 (May 25) 1928.

A child, aged 3 months, was in good condition, but presented a peculiar high pitched cough, with some difficulty in expiration. Tuberculin reactions were negative. A month later, the cough still being present, the mother was induced to place the child in the hospital. A roentgenogram of the child's chest showed a coin at the level of the bifurcation of the trachea. Duken believed that a diagnosis of foreign body at the level of the bifurcation of the trachea could be diagnosed by these symptoms.

The Treatment of Heubner-Hertershen (Celiac) Disease. R. von Steinen, Arch. f. Kinderh. **84**:144 (May 25) 1928.

Von Steinen's diet for celiac disease consists of the following: for breakfast, 250 Gm. of Eweissmilch or sour milk; midmorning, 100 Gm. of curds and sour milk; noon, 200 Gm. of 10 per cent rice water with curds and sour milk, and a piece of lean meat, with mashed potatoes; midafternoon, 250 Gm. of sour milk and zweiback; evening, 100 Gm. of curds in sour milk, a piece of white bread with a lean sausage, one egg, and from two to ten bananas. Five cases were reported in which good results were obtained with this diet.

Sanford, Chicago.

Liver Therapy in Nurslings' Anemia. J. Tuscherer, Monatschr. f. Kinderh. **39**:264, 1928.

A liver diet is of value not only in pernicious anemia, but in the various other anemias of infancy and childhood.

ROENTGEN DIAGNOSIS OF PLEURITIC PROCESSES IN INFANCY AND CHILDHOOD. HERBERT SCHOENFELD, Monatschr. f. Kinderh. **39**:385, 1928.

In a comprehensive article with helpful illustrations, Schoenfeld describes the roentgen diagnosis of pleuritis costalis, pleuritis diaphragmatica, pleuritis interlobaris and pleuritis mediastinalis. An abstract of this study would not be of value to the pediatrician without the accompanying illustrations.

TREATMENT FOR EMPYEMA IN CHILDREN WITH BOUILLON FILTRATES OF BESDREDKA. VLADIMIR MIKULOWSKI, Monatschr. f. Kinderh. **39**:472, 1928.

Twelve children were treated for empyema with injections of pneumococcus bouillon filtrates into the pleural cavity. The filtrate was obtained by passing a 7 to 8 day old culture through a Chamberland filter. After the removal of the pus by thoracentesis, the bouillon was injected in amounts of from 2 to 20 cc. The number of injections varied from one to eight. Ten of the twelve children made perfect recoveries.

LIVER TREATMENT OF ANEMIA IN NURSLINGS. OSKAR HERZ, Monatschr. f. Kinderh. **40**:116, 1928.

In the secondary anemias of nurslings, the liver powder (Merck) proved much more effective than various extracts. Recovery took place in about four weeks. This treatment did not influence the anemia caused by infections or malignant tumors. Increase in the amount of hemoglobin and red cells followed in an orderly fashion, with improvement in general nutrition. The combination of liver and irradiated ergosterol was especially favorable.

ANURIA DUE TO BILATERAL KIDNEY STONE IN A SIXTEEN MONTH OLD BOY. RUDOLPH STOHR, Monatschr. f. Kinderh. **40**:124, 1928.

An autopsy in a patient with anuria disclosed the fact that the kidney stones were pure calcium oxalate.

THE DIFFERENTIAL DIAGNOSIS OF BRONCHIAL ASTHMA IN CHILDHOOD. ALICE HORWITZ-LAUDERBACH, Monatschr. f. Kinderh. **40**:216, 1928.

Two diseases in childhood which are frequently confused are bronchial asthma and spastic bronchitis. The characteristics of bronchial asthma are: (1) onset after nursing period; (2) origin in familial characteristic of the disease; (3) association with the exudative diathesis; (4) no history of preceding infection, and (5) frequent recurrence of the attacks.

The characteristics of spastic bronchitis are: (1) onset in infancy; (2) no hereditary factor; (3) no association with the exudative diathesis; (4) usually follows infection of the upper respiratory tract, and (5) often only one attack.

Starting out with these points of differentiation, the author has made a careful review of the literature, which contains a number of symptoms described as rudimentary forms of asthma. Among them are a certain type of cough which is loud, barking and continuous and often leads to the diagnosis of croup or whooping cough; a mild dyspnea, accentuated by physical work, and asthmatic bronchitis.

The author then reviews a series of thirty-five cases studied over a period of time. She does not find any sharp distinction between bronchial asthma and spastic bronchitis; she suggests that spastic bronchitis be classified as one of the rudimentary forms of bronchial asthma.

PYURIA COLI. A. ADAM, Monatschr. f. Kinderh. **40**:**251**, 1928.

Of forty-eight patients with bacteriuria, forty-four had *Bacillus coli* in the urine. Of these, thirty-four contained a colon bacillus of a specific biologic type. In the fermentation reactions, this pyuria colon bacillus differed from the dyspepsia

colon bacillus in its action on sorbite. In fermentation of lactose, saccharose, sorbose and dulcite, the reactions of the two strains were identical. Immunologic reactions, as tested on guinea-pigs, also showed specific difference in the two organisms.

GERSTLEY, Chicago.

ACUTE ALEUKEMIC LYMPHADENOSIS. O. HERZ, Ztschr. f. Kinderh. **44**:255 (Oct.) 1927.

Herz reports a case of aleukemic lymphadenosis in which especially the liver, spleen, kidneys and stomach were implicated, while the lymph glands were minutely attacked. In general, a lasting leukopenia was present; only by external influences did transiently increased numbers of leukocytes occur. The highest number was 25,000 and the lowest, 800. The outstanding anemia was much improved by one transfusion of blood.

EMERSON, Boston.

UROGENITAL DISEASES IN INFANCY: III. PROGNOSIS OF PYURIA. S. LEVY, Ztschr. f. Kinderh. **45**:643 (June) 1928.

In a series of sixty-seven cases of pyuria, twenty of them in boys, the disease manifested itself in fifty-eight patients within the first year of life. In 55 per cent of the cases, pyuria was associated with other diseases, especially those of the respiratory organs. A frequent combination of pyuria and disturbances of nutrition, or an especially frequent incidence in breast-fed infants, however, could not be established. Forty-six per cent of the patients were cured and 20 per cent died. Although, therapeutically, the chief emphasis was laid on efficient nourishment and although a cure was obtained in seven of eleven patients who were not treated with drugs, intravenous administration of a colloidal silver preparation in a number of cases proved valuable. Thirty-one of the patients were examined after six or seven years; in twenty-one of these, the urine did not display a pathologic condition. In three cases numerous leukocytes were found, and in seven an occasional leukocyte, red cell or cast, was evidence of functional weakness of the kidney. A typical cystitis, then, was found in only three of ten cases. In two of these, the disease had existed for several months and in a third, for four years. Of the ten patients who gave a positive reaction on reexamination, four had been discharged originally as well, two as improved and four as not improved. Five patients whose urine was normal on the follow-up examination had been discharged formerly as not improved, and four patients who had been discharged as improved were now well. These figures show that patients with pyuria usually are cured spontaneously.

MULTIPLE OSTEOMYELITIS WITHOUT SEVERE GENERAL SYMPTOMS IN AN INFANT. DORA KARPLUS, Ztschr. f. Kinderh. **45**:732 (June) 1928.

Two cases of inflammation of the upper jaw, both osteomyelitic, are reported in infants. In the first case, the inflammation remained localized in the upper jaw and ran a typical course for the loss of the embryo of a tooth in the discharge. The second case showed multiple osteomyelitic foci in the upper jaw, ilium and the bones of the extremities; the disease ran a mild course with a complete lack of general symptoms.

EMERSON, Boston.

DEVELOPMENT OF PULMONARY ANTHRACOSIS IN CHILDHOOD. M. J. MADLENER, Ztschr. f. Tuberk. **49**:321, 1928.

This study was undertaken in order to determine whether certain parts of the lung show a predilection for the deposition of anthracotic material. Lungs of forty-four children between the ages of 2 months and 6 years were examined. The result of these studies was that there is no definite predilection in early anthracosis. In the majority of the lungs, deposition of coal pigment was found, even or nearly even, throughout both lungs. Deviations from this general condition were fre-

quently due to pathologic lesions such as scars, adhesions and inflammatory changes. The frequency of such changes in the apical parts of the lungs in adults explains the fact that in later years the apical parts show a predilection for anthracosis. But the primary seeding appears to occur at approximately equal density throughout the parenchyma.

MAX PINNER.

ACUTE RHEUMATIC ENDOCARDITIS WITH INCREASED P-R INTERVAL. PAUL IVERSON, Ugesk. f. Laeger. **90**:959, 1928.

The significance of the increased P-R interval is discussed with a short review of the literature. The lengthening of the P-R interval is not limited to acute rheumatic fever but may be present in pneumonia, diphtheria and typhus, although much less frequently.

The author presents one case of acute rheumatic fever in which the P-R interval was increased to almost three times its normal value. Fifteen days' stay in the hospital had reduced the interval to normal.

SCHLUTZ, Minneapolis.

Nervous Diseases

DRAINAGE OF THE CISTERNA PONTIS LATERALIS IN OTOGENIC MENINGITIS. ALFRED LEWY, Arch. Otolaryng. **7**:614 (June) 1928.

The author gives a short account of the history of this operation and "is unaware of any reports of this operation in the American literature." He has overlooked the reports of the operation by Eagleton. He quotes Goerke as follows: "After the radical mastoid operation is performed (all his patients had chronic suppurations; the complete radical operation may not be necessary), the dura of the middle and posterior fossae is uncovered over a considerable area, the operator going back of the sinus in order to get sufficient operative space and to permit some displacement backward of the cerebellum. The bone in front of (mesial to) the sinus and behind and above the facial ridge is then chiseled away. If the labyrinth is infected, the operation is simplified by going through this structure. Then with a septal elevator, he separates the dura from the posterior surface of the petrosa until at the meatus auditorius internus, the cushion-like projection of the cisterna can be seen."

The case of a child with otitic meningitis following chronic otitis is reported. "The spinal puncture did not elicit any fluid," so that one has no way of knowing whether there was any active infection in the meninges, although the author reports that on opening the cisterna pontis lateralis, a flow of curdy pus was obtained. The child recovered.

In the second case, spinal puncture revealed a turbid fluid under pressure. The cells numbered 9,280, but a bacterial count was not made. The patient died.

The reviewer feels that neither of the cases reported in the aforementioned article are of statistical value, because, as the author has noted in his comment, "The laboratory investigation was faulty," there being no reports of culture or bacteriologic studies.

"The operation is distinctly an otologic procedure. It appears to be a logical approach for drainage in otogenic meningitis, and perhaps for other types, with a reasonable hope for recovery if the infection is still limited to the posterior fossa, although beyond the ear spaces. Undiagnosed depots of pus may be disclosed, and if the operation cannot cure patients with generalized forms of the condition, at least the persistent cerebrospinal drainage seems to relieve suffering and may obviate the necessity of repeated spinal punctures. The Haynes' operation necessitates a separate approach at the foramen magnum.—Perhaps Portman's saccus operation will prove to give sufficient access. The dura is easily separable until one nearly reaches the cisterna, but pathologic conditions may change this. Incidentally, on the cadaver, the jugular bulb was accessible in front of the lateral sinus without endangering the facial nerve."

HUNTER, Philadelphia.

THE PROGNOSIS AND THE LATE RESULTS OF POSTENCEPHALITIC RESPIRATORY DISORDERS. W. ALDREN TURNER and MACDONALD CRITCHLEY, J. Neurol. & Psychopath. **8**:191 (Jan.) 1928.

The authors state that although the number of cases which form the basis of their article is too small to justify definite conclusions as to prognosis, it is possible that the twenty-nine cases investigated constitute a representative example of postencephalitic respiratory disorders in general. Almost every variety of known breathing anomaly was represented. Nearly one half of the cases either have ceased to show any respiratory disorders or else have shown them to an attenuated extent. An equal proportion of cases remained unchanged over a period of time extending up to three years. Two patients died while still giving evidence of a respiratory disorder. It appears that the character of the breathing anomaly does not materially alter the prognosis. The proportion of cases in which there was recovery appears to be greater in the cases with a progressive parkinsonian state than in those without the manifestations of paralysis agitans. Certainly, numerous physical and psychic stimuli may temporarily influence the severity of the disorder, but there is no evidence that these factors are other than temporary. The recovery rate apparently does not depend on any particular treatment; improvement seems to come spontaneously.

FAVILL, Chicago.

POLIOMYELITIS IN WISCONSIN IN 1927. H. M. GUILFORD, Wisconsin M. J. **27**:310 (July) 1928.

Deductions made from a summary of 155 cases of poliomyelitis showed a mortality of 19.3 per cent. About 35 per cent of the patients were under 5 years of age and 7.6 per cent were over 20. Reflexes were normal in 1.8 per cent. In five of the patients, the condition was diagnosed as nonparalytic. Serum used in seventeen cases did not cause a marked change in the results.

THE AIM OF MEDIAL PSYCHOLOGY. ANNETTE MCINTIRE, Wisconsin M. J. **27**:349 (Aug.) 1928.

Medical psychology accomplishes most when applied during the basic preschool period. Habit clinics and nursery classes for young children solve many behavior problems and are in increasing demand. Parents need insight into child psychology as well as instinct, in order to equip the child with understanding and control if he is to avoid the neurasthenic type of difficulties common to adolescence.

JANNEY, Milwaukee.

ENCEPHALITIS PERIAXIALIS DIFFUSA: SCHILDER'S ENCEPHALITIS. A CRITICAL REVIEW. C. P. SYMONDS, Brit. J. Child. Dis. **25**:83 (April-June) 1928.

Collier and Greenfield's case, observed in 1902 but not reported until 1924, as well as Schilder's case reported in 1912, are reviewed. A case reported by Pierre Marie and C. Foix is cited as the first example in the literature of spontaneous arrest of the disease in its active stage with subsequent pathologic verification.

In 1928, Symonds published evidence in *Brain* (**51**:24 [March] 1928) to substantiate the familial incidence of the disease. Three children of one family were affected. One of the children, a boy aged 6 years, died after six months of illness; autopsy showed the characteristic picture of Schilder's encephalitis. In a sister aged 20 and a brother aged 11, the evidence is not absolutely conclusive. Ferraro described the disease, proved by postmortem examination, in a sister and two brothers; the onset in all three cases was between the ages of 20 and 30. These patients showed mental deterioration, weakness, ataxia, primary optic atrophy, scanning speech and exaggerated deep reflexes.

It is now recognized that the starting point of the spreading lesion is not necessarily in the occipital white matter but may be in some other part of the brain; also that the disease may be familial, may commence at any age, may be rapidly progressive to a fatal issue, may progress slowly or may become arrested.

Externally, the brain appears normal. On section the central white matter of the affected lobes appears gray and may show areas of actual softening, while the subcortical strip of intact white matter stands out between the gray matter of the cortex externally and the gray degenerated areas within. Histologically, the distinction is clear between healthy and demyelinated zones. Although the primary change is in the myelin sheaths, the axis cylinders do not escape and the term "encephalitis periaxialis," suggested by Schilder, is therefore misleading. The histologic picture varies somewhat with the stage at which death has occurred.

HYDROCEPHALUS: A STUDY IN PHYLOGENY AND PATHOLOGY. SIR JOHN BLAND SUTTON, Lancet **215**:687 (Oct. 6) 1928.

The author states that congenital hydrocephalus and congenital hydronephrosis are parallel conditions; they arise during intra-uterine life. The epithelium of the kidney and the choroid plexus of the brain are active about the fourth month of intra-uterine life. The choroid plexuses perform that function for the brain which the renal epithelium exercises for the body generally. For fifty years, the author sought for an anatomic relationship between the ventricular cavities of the brain and the labyrinth of the ear believing that the route lay through the lateral recesses of the fourth ventricle. In his studies of the embryos of dogfish, in 1927, Leo Alexander found that at one point the walls of the endolymphatic cavity and the fourth ventricle are separated only by a thin tense membrane; he concluded that "the recessus lateralis is phylogenetically an old organ." Many examples of congenital hydrocephalus are due to prenatal bilateral occlusion of the lateral recesses of the fourth ventricle of the brain.

LANGMANN, New York.

ABSCESS OF FRONTAL LOBE: POSTMORTEM FINDINGS IN CASE SHOWN AT A PREVIOUS MEETING OF THE SECTION. D. W. WINNICOTT and ELIZABETH O'FLYNN, Proc. Roy. Soc. Med. **21**:56 (May) 1928.

The patient was 6 years of age at the time of her death in January, 1928. She had been under observation since January, 1925. The only symptoms complained of in the beginning were severe headaches and retarded mental development. There was also a change in fat distribution and a certain amount of so-called sexual precocity. As the mother had active phthisis, tuberculosis was suspected.

In January, 1928, acute symptoms pointed directly to intracranial disease, and tuberculous meningitis was suspected. Lumbar puncture did not confirm this diagnosis, and the patient died before further investigations could be made. There was no history of vomiting. The postmortem examination revealed a large abscess in the right frontal lobe of the brain, involving the whole anterior half of the right hemisphere. The convolutions were flattened. The cavity contained a quantity of blood-stained pus. A streptococcus was present in direct films and also in the culture. The ethmoid, sphenoid and mastoid sinuses were healthy, and an obvious primary focus of infection could not be found.

WILLIAMSON, New Orleans.

CEREBRIFORM ASPECT OF THE SKULL IN RADIOGRAPHY OF TUMORS OF THE BRAIN IN THE YOUNG. NOBECOURT, HAGUENAU and BIZE, Arch. de méd. d. enf. **10**:581, 1928.

Diagnosis of tumors of the brain by means of x-ray examination, even with the refinements afforded by the Potter-Bucky diaphragm and by stereoroentgenograms, is unsatisfactory. If the calcium in the tumor mass is sufficient to throw a direct and visible shadow and if the tumor has produced an erosion or an abnormal densification of the cranial bones through pressure, radiography can furnish a diagnostic topography of absolute precision. The latter signs are exceptional; it does not follow, however, that in their absence, x-ray studies are without value.

In the absence of localizing phenomena, there are certain symptoms produced by hypertension which may be of genuine significance in the differential diagnosis. The increased intraventricular pressure produces in children, but rarely in adults, a constant sign which is known as the cerebriform aspect of the skull. This peculiar radiologic entity has been known for some time; it has been discussed freely by Klose, Fittig, Strater, Benedikt and others.

In anteroposterior views as well as those in profile and particularly in stereographic roentgenograms, one is struck immediately by the absence of homogeneity in the cranial shadow. This shadow, which normally is absolutely uniform at the level of the vault, occurs here as a dappling of clear zones with darker ones, appearing to outline on the cranial box the topography of the cerebral convolutions. It is especially clear in the frontal region, where it appears hammered out; some writers have referred to it as the "digital impression." At the convexity, this cerebriform aspect is less pronounced; it is more linear in character and is seen only when symptoms of intracranial pressure have existed for a considerable period. The authors feel that it is entirely probable that these alterations are produced by direct pressure of the convolutions on the cranial bones, the imprint being most pronounced on those bones which even in the normal dry state show similar digital markings. This assumption has not been confirmed at the autopsy of children dying of tumor of the brain; it has been verified, however, in a case of craniofacial dysostosis reported by Apert. In addition, injection of the ventricles of an infant cadaver has given an identical picture.

Nine cases with accompanying roentgenograms are reported.

AMESSE, Denver.

THE ALBUMOSES AND THEIR RELATION TO EPILEPTIC AND INSULIN CRISIS. GEROLAMO CUNEO, Biochim. e terap. sper. anno dodicesimo, fascicolo terzo, 1926.

The author, after an exhaustive investigation, observes that the albumoses found in epileptic patients behave like insulin. When injected into the veins of dogs, they produce convulsions, lowering the blood sugar as low as from 0.5 to 0.4 per thousand, precisely as happens with convulsions induced by insulin. He finds similar hypoglycemia in epileptic patients just before or during the convulsive seizure, and injections of dextrose have produced a complete suppression of the attacks. He is inclined to think that insulin is an albumose or a substance analogous to albumose.

When the albumoses are precipitated they assume either a waxy or a flocculent form. The waxy precipitation produces convulsions and lowers the blood sugar as low as from 0.5 to 0.4 per thousand. The flocculent precipitant does not produce convulsions, and the glycemia is never below 0.57 per thousand; it causes only toxic phenomena. These toxic symptoms correspond to those found in certain epileptic patients without convulsive seizures.

When subcutaneous (and, as Dr. Osnato has found, intravenous injections of from 10 to 15 per cent) injections of 10 per cent dextrose were administered to twenty patients with daily epileptic seizures the attacks were suppressed for twenty-six days. After this time, three patients had a remission of the convulsions, while a few others experienced milder attacks.

Analogous action was observed between injections of insulin and dextrose not only in rabbits but also in diabetic patients.

The author finds that injections of dextrose suppress epileptic convulsions in the same manner that the convulsions produced by the albumoses and insulin are suppressed.

VINCIGUERRA, Elizabeth, N. J.

PARKINSONISM IN INFANCY. MARTINEZ VARGUS, Med. de los ninos **29**:161 (June) 1928.

Parkinson's syndrome is described in a girl, aged 13 years, whose history reveals a disturbance in control of muscles as early as the third year; the con-

dition, however, had been developing since the age of 6. The syndrome is dependent on a lesion, toxic, infectious or neoplastic in nature, which produces destruction of the motor cells of the corpora striata and the locus niger. Scopolamine is used for the relief of symptoms, but the disease is regarded as incurable.

DWYER, Kansas City, Mo.

EXPERIMENTAL TRAUMATIC HYDROCEPHALUS. M. HASHIGUCHI, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **29**:109, 1927.

Because ventriculography has demonstrated hydrocephalus in patients suffering from traumatic neuroses, an attempt was made to produce hydrocephalus in dogs. After the animals were deeply anesthetized, the heads were tapped with a lead hammer one hundred times on each side. In spite of care, slight fractures resulted in two of the seventeen dogs. The outcome is much more of a contribution to cerebral concussion and contussion than to hydrocephalus, for edema followed by necrosis of nerve cells and an atrophy of the brain evident grossly were found. Some proliferation of subependymal neuroglia was also noted. This would probably help to produce hydrocephalus by narrowing the passage outward of the fluid in the ventricles. Hashiguchi suggests that the time of observation, three months, was not long enough to allow hydrocephalus to develop. A slight hydrocephalus was also found in one of four dogs used as controls.

E. R. LE COUNT.

ENCEPHALITIS COMPLICATING A PARATYPHOID-B INFECTION IN INFANCY. GUSTAV THEWALT, Monatschr. f. Kinderh. **39**:271, 1928.

An infant suffering with paratyphoid B infection developed paralyses, which led to a diagnosis of complicating encephalitis. This diagnosis was confirmed by the disappearance of the paralyses.

LATE SPASMOPHILIA. HANS SCHLACK, Monatschr. f. Kinderh. **40**:89, 1928.

In a child, aged 6 years, with typical tetany, the attacks were controlled with 10 grains (0.65 Gm.) of calcium chloride daily. Ultraviolet rays proved valueless. The fact that the condition was so little influenced by irradiation would suggest the tetany to be of the adult type. For such an intermediate form, the writer offered the term "puerile tetany."

GERSTLEY, Chicago.

CLINICAL REPORTS. H. R. KROGSGAARD, Ztschr. f. Kinderh. **44**:400 (Oct.) 1927.

1. *Three Cases Resembling Meningitis.*—The first, a case of procephalus internus and of infection with *Proteus vulgaris,* occurred in a girl, aged 5 weeks, who was sick for more than a month with a slightly enlarged head and convulsions. The pathologist found thin, gray-green, foul pus in all the ventricles and even in the lymph spaces of the brain, which, according to Krogsgaard, is very rare. *Proteus vulgaris* was found in cultures taken from the spinal fluid and also from the urine and feces.

A case of cryptogenic meningitis occurred in an infant, aged 9 months, who recovered after an illness of three weeks. There was clinical evidence of meningitis. The spinal fluid contained thousands of lymph cells and a fibrin clot, but did not show any globulin. Bacteria were not found either by smear-culture or by inoculation of guinea-pigs. Whether or not the underlying cause was stomatitis could not be determined. The spinal fluid showed the symptoms of tuberculous meningitis, with the exception of the sugar content, which was not so much diminished.

A case of meningismus occurring during the course of enteritis was the third of this group. A boy, aged 24 months, during the course of enteritis developed intoxication which continued and increased for fourteen days after the cessation of the diarrhea, until a keratoconjunctivitis appeared. Such a typical picture of meningitis developed that tuberculosis was suspected. The course of the disease was almost afebrile, and the spinal fluid was normal. The patient recovered.

2. *A Case of Congenital Folding of the Duodenum.*—An infant, aged 3 weeks, died with symptoms of an incomplete obstruction of the intestinal tract. Autopsy disclosed stenosis caused by a fold in the duodenum, a circumstance which is unique in the literature and without ascertainable cause.

EMERSON, Boston.

CARCINOMA OF THE CEREBELLUM IN AN INFANT ONE YEAR OLD, PRESENTING A PICTURE OF MENINGITIS. H. FUHRMANN, Ztschr. f. Kinderh. **45**:725 (June) 1928.

An infant, 1 year old, sick for fourteen days with vomiting, diarrhea and drowsiness, was thin and pale and cried a great deal. She had paralysis of the right levator palpebra superior and of the rectus medialis, fixed pupils and a right knee reflex less than the left but no stiffness of the neck and no Kernig's sign. The spinal fluid obtained under a pressure of 180 mm. of water showed a trace of albumin, fifty cells, mostly lymphocytes, and no bacteria. The head increased in circumference during the last weeks, the infant dying in two months. At autopsy, the pathologist found not only an external and internal hydrocephalus with cloudy meninges and cloudy spinal fluid, but a cancer in the left cerebellar hemisphere.

EMERSON, Boston.

Diseases of the Ear, Nose and Throat

HAEMANGIECTATIC HYPERTROPHY (PARKES WEBER). A. M. H. GRAY, Proc. Roy. Soc. Med. **21**:65, 1928.

This was a case of extensive congenital nevoid condition of the right lower leg in a boy, aged 10½. The abnormality had been noted since he was 2 or 3 years old. The right leg was larger and darker than the left; dilated veins were present in the region of the knee. The right lower leg was 4.5 cm. longer than the left, most of the increased length being in the leg, not in the thigh. The increased length of the femur was 1 cm., and below that 3.5 cm. There was also a difference in girth, that of the right leg being greater by 1 cm. Pulsation in the right femoral artery was greater than in the left. On the right leg this could be felt down to the popliteal space; on the left, only 2 inches below the groin. There was an area of abnormal pulsation internal to the patella, and extending down the anterior surface of the leg. The pulsation disappeared on compression of the femoral artery. There was a thrill in the right femoral artery and over the enlarged vessels under the patella which Sir Thomas Lewis thought was of arterial origin. There was also distinct pulsation in the veins. Over the femoral vessels there was a continuous murmur. The right ankle was of the same temperature as the left, but in the region of the right knee there was a difference of 2.7 C., and at the right thigh 2.1 C. The right leg was 3.75 C. hotter than the other. Obliteration of the right femoral artery had much greater effect on the pulse rate than obliteration of the left femoral artery, indicating lesser resistance to outflow on the right side. There was a general increase in the circulation of that leg, and probably a communication existed between arteries and veins.

GUY, Pittsburgh.

MASTOIDITIS AS SEEN IN INVESTIGATIONS OF WHOLE TEMPORAL BONES AND BONE SPLINTERS. MAYER, Ztschr. f. Hals-, Nasen- u. Ohrenh. **18**:628, 1927. (From the Proceedings of the German Otolaryngologic Society.)

In a well illustrated article, the author takes issue with some heretofore accepted ideas, and comes to the following conclusions:

Mastoiditis is initiated by an exudative inflammation originating in the tympanic cavity and progressing by continuity through the antrum, running its course almost entirely in the air-containing spaces.

As early as the fourth day, in some cases, besides the exudative reaction there may be seen resorption of bone by osteoclasts in the small bone vessel spaces,

also new formation of bone as osteoid seams in both the vessel spaces and the pneumatic spaces, although the resorption and new formation are scant.

The exudative stage predominates for about a week and is then replaced by the proliferative stage, indicated by the formation of granulation tissue. During the granulation stage, there is resorption of bone. This seldom occurs by osteoclasis of the walls of the pneumatic cells, but occurs principally in the vessel spaces and usually in the newly formed vessel spaces.

Cortical perforation takes place through the outgrowth of granulation buds.

The disease process is in the region of the pneumatic spaces, progressing through the septums and cortex. Hematoplastic and fatty marrow as found in nonpneumatic mastoids is not primarily involved, but is involved when pneumatic cells are scattered through marrow spaces.

Demarcation and healing of suppuration can occur, but often there may be extension of the suppurative process into the depths of a bone, where it may be difficult to gain access for operation. In streptococcus mucosus infections, it was frequently noted that the process extended along the posterior surface of the pyramid toward the front and from there broke through the dura; this should give some guidance in operative work.

There are some cases which are largely exudative and others in which proliferation of inflammatory tissue predominates. In the first group are the stormy types, e. g., in influenza, and in the second the insidious types mostly produced by streptococcus mucosus. Between these two types are many gradations.

LEWY, Chicago.

THE DETERMINATION OF CALCIUM IN THE BLOOD SERUM OF PATIENTS SUFFERING FROM OTOSCLEROSIS. C. F. LINDEMANN, Norsk. Mag. f. Laegevidensk. **89**:223, 1928.

The author has not found a lowering in the amount of the serum calcium in patients suffering from otosclerosis. Calcium therapy in these patients is therefore not justified.

TOVERUD, Oslo.

Diseases of the Skin

THREE CASES OF SCLEROEDEMA ADULTORUM BUSCHKE. LEIPZIG VON GRAEVENITZ, Monatschr. f. Kinderh. **39**:257, 1928.

The author describes three cases in which the symptoms began with impetigo.

A CASE OF MULTIPLE GRANULOMA ANNULARE IN CHILDHOOD. LEO LEMEZ, Ztschr. f. Kinderh. **44**:328 (Oct.) 1927.

Histologic evidence confirmed the diagnosis of multiple typical foci of an annular granuloma, with partial spontaneous reformation, in an otherwise healthy boy, aged 2½ years, and free from tuberculosis. Complete healing of the condition followed periods of local freezing with ethyl chloride, two or three times every forty seconds, at intervals of five days, with the simultaneous exhibition of arsenic. Tuberculosis is denied as a cause of annular granuloma, since annular granuloma occurs most frequently in early childhood when tuberculosis is infrequent and since it seldom occurs in senility when tuberculosis abounds. Tuberculosis is further excluded by the discovery of characteristic symptoms, by the negative results from animal inoculations and finally by the complete freedom of the patient from tuberculosis. Positive skin reaction after the insertion of material obtained on excision in the same person appears to refer to a specific allergic condition of the skin, brought about by the overcoming of the annular granuloma. Whether or not there was an after-reaction in three weeks following the inoculation, the authors could not decide on the basis of their cases. For the evidence of a specific allergic reaction in annular granuloma, the inoculation of a control group of children with inactive material would be necessary, but this is impossible.

EMERSON, Boston.

Surgery and Orthopedics

INTUSSUSCEPTION. W. E. HARTSHORN, Boston M. & S. J. **197**:1297 (Jan. 12) 1928.

The author reports twenty-eight cases of intussusception in children, and the cases were classified according to the extent of the condition. It extended to the ascending colon in seven; to the splenic flexure in seven; into the sigmoid, in eight; it appeared at the anus in one, and was of the self-reducing type in three. Eight children died; of these, two were admitted too late for operation; the other six deaths were due to delay in diagnosis. One patient developed an obstruction in a loop of the small intestine nine days after operation but recovered after a resection with lateral anastomosis.

The anesthetic in all cases was ether administered by the drop method. Up to the present time, no recurrences have been reported. The author believes that there are three predisposing factors: (1) an unusually mobile cecum or ileum, which is common in infancy; (2) tumor of the ileum near the ileocecal valve; (3) some factor producing hyperperistalsis, such as an obstructing band, a Meckel's diverticulitis, a typhoid or tuberculous ulcer, or any other inflammatory condition.

APPENDICEAL ABSCESS: TREATMENT OF THE APPENDIX. JOHN HOMANS and JOHN H. POWERS, New England J. Med. **199**:319 (Aug. 16) 1928.

An appendical abscess is a suppurative process due to perforation of the appendix and firmly walled off and palpable. Removal of the appendix for this condition is sometimes unwise and occasionally impossible. This difficulty may be due to one or both of two factors: the situation of the abscess, and the uncertain relation between appendix and abscess.

The cecum lies, as a rule, in the right iliac fossa, the appendix pointing upward and inward behind the ileocecal junction. The remarkable variation in length and the extreme mobility of the appendix, however, permit it, or some part of it, an astonishing range. An abscess, for instance, which is usually formed in the right iliac fossa, may appear in the right renal fossa, in the subhepatic or subumbilical region, or in the pelvis. Eccentric abscesses of this sort are most often found in the pelvis, usually on the right, but sometimes mesially or even on the left; next often, they appear in the right renal fossa. They may be in contact with the anterior abdominal wall or so deeply situated that a considerable area of normal peritoneal cavity must be traversed to reach them. There is, therefore, danger of spreading infection if they are laid widely open in a search for the appendix itself.

A perforation may occur at any point in the appendix, or the whole organ may become gangrenous. If the appendix lies within the abscess it can usually be discovered and removed; if it is embedded in the walls of the abscess, it can only occasionally be found and if it remains largely outside of the abscess, it cannot be discovered without exploration outside of the infected field. In any event, removal of the appendix requires a considerable incision which will become contaminated, much to the detriment of the wound in the abdominal wall.

As a rule, when an abscess has been opened, the appendix is searched for and may be found. If a brief search is vain, however, the abscess is drained, and the diseased organ is left in situ.

Eccentric abscesses, such as form in the right flank or pelvis, are likely to include only the distal portion of the appendix. Perhaps one in five recurs after simple drainage. They can be treated by initial drainage through a short incision, followed, when the discharge has greatly diminished but before the sinus has healed, by removal of the appendix through a second incision made at McBurney's point. In most instances, little difficulty will be experienced; firmly healed wounds will be left and the possibility of recurrence of the appendicitis will be eliminated. Such treatment is not possible when the abscess is situated in the region of the

cecum. Unless the appendix can be removed from such an abscess at the initial operation, the patient must return for an interval operation or risk a recurrence which happens in one out of five patients.

GENGENBACH, Denver.

CHRONIC OSTEOMYELITIS IN CHILDREN. W. COURTIN, Arch. f. Kinderh. **84**:125 (May 25) 1928.

In 320 cases of chronic osteomyelitis, 27 per cent of the infections were located in the tibia, 18 per cent in the femur, 5 per cent in the short bones and 3 per cent in the bones of the head. The exciting organism was, in the majority of cases, *Staphylococcus aureus*. The next in order were the streptococcus, the pneumococcus and *B. typhosus*. The streptococcus and the pneumococcus were more common in infants and young children.

SANFORD, Chicago.

Miscellaneous

PNEUMONOGRAPHY AS A DIAGNOSTIC AID IN CHILDREN. COLE B. GIBSON and WILLIAM E. CARROLL, Am. Rev. Tuberc. **18**:26 (July) 1928.

While stereoscopic roentgenograms will usually yield the essential x-ray data for the diagnosis of pulmonary disease, further information is necessary in certain cases to clarify the clinical picture. Here pneumonography serves a useful purpose, especially in the differentiation between tuberculous and nontuberculous conditions of the lungs. The authors describe the technic for administering iodized oil 40 per cent by the subglottic method, which they prefer for children. They use smaller amounts in young children and adolescents than are usually suggested, and urge that roentgenograms be taken promptly after the injection of the oil and at varying intervals afterward.

Bronchiectasis is often difficult to diagnose from the symptoms, physical signs and the usual roentgenograms which often seem to be at variance with the physical signs. Significant markings on the lungs may be obscured by thickened pleura or shadow of the heart. After injections of iodized oil 40 per cent, however, the diagnosis of bronchial dilatations becomes relatively simple.

This method of examination may yield important information in the diagnosis of abscess of the lung, although the manifestations may not be of such positive value as in persons with bronchiectasis. If the oil can find its way into the cavity of the abscess, its existence and location are easily determined. This is not always possible, since the cavity may be filled or the bronchus leading to this area may be constricted.

In other bronchopulmonary conditions, such as stenosis of the trachea or bronchi, bronchopulmonary fistula, old empyema with formation of a sinus, new growths, and certain excavating diseases of the lungs, valuable diagnostic data may be obtained by recourse to this procedure.

In the experience of the authors harm has not followed the injection of this oil. Iodism is possible if the oil is swallowed and subjected to the action of the intestinal secretions. In two of the patients studied, however, who certainly swallowed as much as from 10 to 12 cc. of the oil, iodism did not occur.

SMITH, Ogden, Utah.

COMMON MISTAKES IN THE DIAGNOSIS AND THERAPY OF DISEASES OF CHILDREN. ALAN BROWN, Canad. M. A. J. **19**:313, 1928.

The author discusses briefly the following conditions which he found to be either frequently overlooked in diagnosis or incorrectly treated: hemorrhagic disease of the new-born, cyanosis in the new-born, enlarged thymus, fever of inanition, pyloric stenosis, tetany, scurvy, intussusception, acute intestinal intoxication, mongolian idiocy and cretinism, heart murmurs, otitis media, pyelitis, ammoniacal diaper, retropharyngeal abscess and roseola infantum. The outstanding symptoms and the most effective treatment is given for each condition.

MOORE, Omaha.

SUNLIGHT AND CHILDHOOD. SALEEBY, Rev. internat. de l'enf. **6**:483, 1928.

The author reviews the interesting history of the use of sunlight in medicine from the time of Bonnet of Lyons, who cured tuberculosis of the bones and joints in children nearly a hundred years ago, to Rollier and his memorable work on rickets.

An appeal is made for Saleeby's so-called heliohygiene of pregnancy in the prevention of antenatal rickets, for more use of sunlight during the summer months in England and for a wider use of ultraviolet ray therapy in these months during which England is enshrouded in its curtain of smoke. Even more important than the problem of rickets is that of tuberculosis. Saleeby recommends the expenditure of less in the equipment of the laboratory and more in the abolition of slums and soot. He believes that open air schools should be encouraged everywhere and the architecture of the rest of the schools radically changed.

AMESSE, Denver.

THE PROBLEM OF INSTITUTIONAL CARE OF OLDER CHILDREN FOR LONG PERIODS OF TIME. J. DUKEN, Arch. f. Kinderh. **84**:96 (May 25) 1928.

Duken does not believe that enough attention is paid to the effect of long institutional care on the future adaptability of a child. Children who undergo extensive operations and long periods of various treatments in institutions acquire a point of view that hampers their adaptability in affairs of life.

MEASUREMENTS OF STRENGTH IN CHILDREN. D. HUMMEL, Arch. f. Kinderh. **84**:132 (May 25) 1928.

Hummel tested the measure of strength in 245 normal children, compared with that in 157 slightly subnormal children. He used the Colin dynometer which consists of hand pressure on an elastic bow. Compared with the adult measurements, both groups showed 65.4 per cent, on the average, for the right hand, and 34.6 per cent for the left. The pressure decreased rapidly in each group with successive trials. In both groups, the fifth trial showed only 5.5 per cent of that of the normal adult.

SANFORD, Chicago.

A SIMPLE METHOD OF DETERMINING THE POSTURAL DEVELOPMENT OF AN INFANT. W. RISCHBIETER, Gesundheitsfürsorge f. d. Kindesalter **3**:45, 1928.

The author has simplified the study of the postural development of the infant. He offers a list of ten different stages of the child's advance in postural ability.

1. Inability of the child to raise the head when he is lying on the abdomen.
2. The ability to raise the head in this position without the use of the arms.
3. The ability to raise the head and chest with the aid of the arms.
4. The use of the feet in the foregoing position which finally results in creeping.
5. The ability to sit if the child supports itself, or is supported by the hands; the back is not straight.
6. The ability to sit upright without assistance.
7. The inability to stand on the feet if held in the proper position.
8. Ability to stand on the feet, if supported.
9. The ability to walk if supported.
10. The ability to walk without support.

The author has found this scheme valuable in his social service work.

THE INCREASING AGE OF THE PRIMIPARA AND ITS EFFECTS ON MOTHER AND CHILD. L. MOLL, Gesundheitsfürsorge f. d. Kindesalter **3**:110, 1928.

The author comments on the increasing age of the primipara in Vienna. The percentage of women who bore their first child between the ages of 26 and 30 increased from 26 to 32 per cent; after the age of 30, from 14 to 27 per cent. This is not due to the fact that women are marrying later.

Moll noticed that there is a large number of these older primiparas who are not able to nurse their children. The differences in temperatures of the skin of the mammary folds and of the axilla make him believe that the breast tissue is active, but that the increase of connective tissue due to the involution of the breast makes it difficult for the child to nurse. The breasts and the nipples are particularly firm in these women, and even children who are known to drink well do not succeed in obtaining any milk.

He believes that prematurity is also more frequent among these women, and he regards this fact as of particular importance because of the difficulty of labor at this age. He attributes many of the defects of intelligence found among children of older couples to these facts.

Last, he finds that the older mother is nervous and tends to produce an environment which may cause behavior problems in the child.

REICHLE, Cleveland.

FAT ANABOLISM IN INFANCY. OSKAR BOSCH, Monatschr. f. Kinderh. **39**:309, 1928.

Experimentation with different methods was made to determine the degree of fat anabolism. The author found that measurement of the fatty wall of the abdomen was the most reliable method. His study shows that there is a greater tendency in female infants to store up fat that in male, while in the latter he noticed greater tendencies toward growth in length. Even in infancy there are alternating periods of deposit of fat and growth in length. In a general way, the children with well developed fatty tissues are superior to the others both in weight and in length. On the other hand, the thinner children tend to grow in height more rapidly than the fat ones but do not gain so well in weight. Morbidity and mortality are somewhat greater in the thin than in the fat group. In a general way, therefore, the thickness of the fatty wall of the abdomen is an index of the biologic condition of the infant.

A METHOD OF DETERMINING THE RESISTANCE OF RED BLOOD CORPUSCLES WITH SMALL QUANTITIES OF BLOOD. HERMANN SCHADOW, Monatschr. f. Kinderh. **40**:276, 1928.

A technic is described which requires 0.1 cc. of blood.

GERSTLEY, Chicago.

THERAPEUTIC RESEARCH WITH HYPHOPHYSIN IN ATONY OF THE STOMACH IN INFANTS AND CHILDREN. E. KOENIGSBERGER and W. MANSBACHER, Ztschr. f. Kinderh. **44**:265 (Oct.) 1927.

Because hypophysin shortens the duration of stay of food in the atonic stomach, by stimulating the perisystolic function, vomiting is diminished. For this reason it is a useful agent for the cure of atony of the stomach. It makes superfluous the hunger cure practiced at the present time, which causes a strain on infants already considerably harmed. If hypophysin alone does not show satisfactory results, a combination of hypophysin and epinephrine, or better, hypophysin and atropine, will stop the vomiting.

THE TECHNIC OF TAKING X-RAY PICTURES IN CHILDHOOD. L. FREUND, Ztschr. f. Kinderh. **44**:393 (Oct.) 1927.

An apparatus is described for holding restless infants in various positions for x-ray work. It is declared to prevent failures by overexposure and to avoid waste of time, material, tubes and money.

EMERSON, Boston.

NATURAL INCREASE OF POPULATION AND ITS FACTORS. KAROL RYDER, Opieka Nad Dzieckiem **6**:287, 1928.

Although the absolute number of the population in a given country is constantly increasing, the percentage of increase from decade to decade at the same

time grows less in all the countries studied. Three factors are concerned in the problem of natural increase: (1) birth rate, (2) death rate and (3) immigration. This analysis concerns itself only with the first two. In all the countries studied, the birth rate is decreasing, and all efforts to prevent this decline are unsuccessful. The death rate, however, is also decreasing, and all measures must be taken to decrease it in order to keep the population of a given country at the desired level.

CREATIVE POSSIBILITIES IN THE ORPHANAGES. M. ELENTUCH, Opieka Nad Dzieckiem **6**:323, 1928.

In most orphanages there is a lack of understanding of the creative possibilities of the children and of opportunity for developing them. The Lodz Orphanage attempts to develop initiative through work which the child in a measure chooses for himself. The children are divided in groups according to their tastes, and a task which lasts about four months is begun. For example, some of the children with old things which were at hand built a small fountain, then, directing the water into a stream, built a water-mill. Such a procedure gives the child not only an opportunity to work with the things which interest him most but an understanding of them and a sense of achievement.

ASSISTANCE TO MOTHERS AND INFANTS OF FRANCE. WANDA TARNOWSKA, Opieka Nad Dzieckiem **6**:328, 1928.

France is a country menaced by depopulation. The protection of children and nursing infants is said to be more developed there than elsewhere. Special laws assist mothers of large families. There is a tendency today to create centers of nursing. Many infants are cared for in the country by wet-nurses who are not competent. In the aid given abandoned infants, one finds all types of care. Ideally, the infant should be placed in a family for care.

THE PROTECTION OF CHILDREN FROM THEIR PARENTS. ADOLF KLESK, Opieka Nad Dzieckiem **6**:334, 1928.

Officials of the recently organized Institution of Hygiene who visit children in their homes find that many children are abused and molested by their parents, particularly by drunken fathers. The gentlest way of intervention is to warn the parents through the school nurse or through the priest, that the name of any brutal father will be publicly revealed. In families in which the children are mentally defective or in which the father is a chronic drunkard, the children should be removed from the home and placed in institutions or with other families.

LESLIE, Evanston.

THE INFLUENCE OF THE SOUTHERN RUSSIAN CLIMATE ON THE CONSTITUTION OF CHILDREN. P. C. MEDOWIKOFF, Russian J. Pediat. **12**:13, 1928.

The author studied the influence of the climate of southern Russia on children from various parts of Russia who were brought to a southern resort and kept there during the summer months. He recorded the changes that took place in the weight, height, circumference of the chest and respiratory excursions of these children. The author then used dermographism and the methods of Ashner, Moro and Dresel to evaluate the changes brought on in the sympathetic and parasympathetic systems. Twelve children showed a change from the sympathetic to the parasympathetic type; seven children did not show any changes, and eight changed from the parasympathetic type to the sympathetic. Children from northern Russian showed a change to the parasympathetic type, while the southern children changed to the sympathetic type. The author believes that these observations may be of importance in the treatment for certain diseases, especially tuberculosis, in which a change to the parasympathetic type is distinctly beneficial to the patient.

GASUL, Chicago.

Society Transactions

CHICAGO PEDIATRIC SOCIETY

Clinical Meeting, Oct. 16, 1928

MAURICE BLATT, M.D., *President, Presiding*

AN ATROPHIC STATE OF PROGRESSIVE FAMILIAL MUSCULAR DYSTROPHY. DR. M. I. MAKLER.

A Bohemian boy, aged 9, had weakness and paralysis of eight years' duration. Two brothers of the child, aged 8 and 10 years, had a similar weakness. According to the history, the delivery was normal. The child was breast fed for nine months, and then received orange juice and cod liver oil. He talked at 2 years of age and walked at 3 years. At 3 years of age, he had an attack of malaise and fever, followed by decided weakness on the right side. A diagnosis of acute poliomyelitis was given to the department of health. The condition became progressively worse until all the extremities were involved, and the patient was confined to bed for two or three years. He now cannot sit up without assistance because of weakness of the erector spinae muscles. He talks slowly in a monotone. The pupils react to light and in accommodation. He smiles constantly. The thyroid is palpable. The upper extremities show marked atrophy, which is more marked in the shoulder girdle. He is unable normally to lift the arm. The pectoralis major muscles are barely palpable. The lower extremities show marked atrophy with reflex contractures and equinovarus of both feet. The hamstring tendons appear to be hypertrophied. The deep reflexes are absent, the superficial present. Muscle, bone and tendon sense is intact. The Stanford-Binet test showed a mental age of 4 years and 11 months, with an intelligence quotient of 44. The chemical examination of the blood gave normal results; blood calcium was present in a normal amount. A roentgenogram of the sella turcica showed a normal condition; x-ray examination of the long bones showed atrophy, with areas of decalcification.

This seems to be a case of familial muscular atrophy of the diffuse type; the two brothers of the patient show the pseudohypertrophic type. The case is presented to show, first, its familial nature, second, its progressive character and, lastly, a possible etiology of infection suggested by the mode of onset and the discovery, by biopsy, of accumulated infiltrations of round cells about the muscle fibers.

PSEUDOCLUBFOOT. DR. A. LEVINSON.

From time to time infants are seen whose lower extremities were strapped the day after birth because of supposed clubfeet and bowing of the legs. Study of new-born infants at the Cook County Hospital reveals that almost all of them have a little curving of the legs and inversion of the feet at birth. This curving and inversion appear to be caused by the intra-uterine position. Infants could be saved much hardship, therefore, if the strapping mechanism, even if merely adhesive tape, were omitted in all but extreme cases of clubfoot.

ACUTE ABDOMINAL CONDITIONS. DR. EDWIN M. MILLER (by invitation).

Intussusception.—Intussusception is encountered frequently. The mortality rate in my experience is about 50 per cent, a figure which compares favorably with others.

In a case of intussusception of twenty-four hours' duration, the clinical picture was typical. Abdominal section disclosed that the intussusception extended to the

descending colon. It was reduced rather easily; after reduction, the terminal 1 inch of the lumen was found to be obstructed. Lumen was not discovered at that point because of the thickening of the entire wall. A lateral anastomosis around the area was performed. The postoperative course was uneventful. Resection in cases of intussusception almost always proved fatal. When the intestine was gangrenous and the obstruction could not be reduced little was accomplished. Death usually followed in a few hours.

Appendicitis.—The most common condition in children is acute appendicitis. It seems peculiar that there should be so much difference of opinion as to the proper treatment in these cases. The proper treatment before rupture seems to be a surgical operation performed as early as possible. If there is rupture with an abscess that is well walled off, there seems to be no doubt that the abscess should be drained and the pus removed, without necessarily removing the appendix. There should be no mortality in these two types. In the third group, in which rupture of the appendix occurs although the process is not localized, there is great difference of opinion as to the proper procedure.

A child was sick for three days, presenting clinically all the evidence of a ruptured appendix, with generalized abdominal symptoms. An immediate operation revealed a ruptured appendix and considerable pus. The appendix was removed and the pus drained. The patient is now in good condition.

These patients should be operated on as soon as they are seen, whether it is two, four or more days after the onset of symptoms, as long as the process is not localized. In order to determine the end-results, statistics must be studied; these mean nothing unless the details of all the cases are known. The statement that the mortality is 2 or 10 per cent means nothing because it includes all types of the condition. I have operated on seventy-one patients in whom a hole through the appendix was present. This did not mean that the appendix was covered with fibrin, and that a milklike material was present in the abdominal cavity; the cases included only those that were gangrenous and gave definite evidence of perforation. In this group there were nine deaths. The patients ranged in age from 9 months to 67 years. Since March, there have been thirty-six patients with ruptured appendix at the Cook County Hospital, all of whom were operated on. Seven deaths occurred. I personally operated on seventeen of these thirty-six patients. There were three deaths, a mortality of 17 per cent. In the seventy-one cases with nine deaths, the mortality was 12.5 per cent. I doubt whether those who believe that these patients should not be operated on could present any statistics which would compare favorably with these. Patients who had not been operated on, and who entered the hospital from three to fifteen days after the onset of symptoms were in such a serious condition that an operation was often of little avail; without an operation, however, death was inevitable.

Intestinal Obstruction.—Another serious condition is intestinal obstruction resulting from appendicitis, evidenced by not only vomiting but the peristaltic waves seen in ordinary paralysis of the ileus.

A girl who had been ill for five days developed signs of intestinal obstruction which made an operation imperative. The appendix was in the center of a mass of intestine, involving half a dozen different links. We removed the appendix, untangled the mass of intestine, and performed an ileostomy above the highest loop involved. There was pus all through the abdomen, even around the spleen. The ileostomy drained for a long time, but when the material drained was directed into a receptacle and not allowed to come in contact with the skin, the patient made a good recovery and the fistula closed.

Another patient, a boy, entered the hospital with all the signs of obstruction. An ileostomy was performed. Drainage was permitted for a month, in the hope that it would close. An anastomosis was necessary, however, between the ileum and the bowel. The fistula closed and the patient is now having bowel movements by rectum.

PATHOLOGIC SPECIMENS. DR. R. H. JAFFE.

The first case showed Dubois sequesters of nonsyphilitic origin. The patient was the fourth child of a woman, aged 25, who experienced a thyrotoxicosis from the second to the seventh month of the pregnancy. Well developed and delivered at full term, the infant developed numerous hemorrhages in the skin, mucous membranes and the conjunctivae after the ligation of the umbilical cord. There was also bleeding from the anus and the mouth. The child died three days after it was born.

Necropsy disclosed not only the hemorrhages mentioned, but a slight enlargement of the thymus which weighed 15 Gm. The organ was firm and deep red, and when cut showed numerous yellowish-white areas of necrosis of the parenchyma. The necrotic material which could be removed easily left small cavities with a smooth lining; microscopic examination revealed these to be composed of stratified epithelium the origin of which could be traced to the ectodermic reticulum which characterizes the thymus.

Since Dubois first described this lesion which now is usually named for him, the opinion most commonly expressed was that it was typical of congenital syphilis (Chiari, Hammar, Hart and Schmincke). In the forementioned case, however, there was nothing which warranted this etiology. The mother had not had any miscarriages; her Wassermann reaction was negative. Bone changes were not found in the distal epiphyses of the femurs of the child and the Levaditi stain failed to demonstrate spirochetes, even in the areas of necrosis of the thymus. The suggested etiology in this case is a septic condition acquired during fetal life; this also accounts for the symptomatic purpura. A nonhemolytic streptococcus was cultivated from the spleen of the infant.

The second case is that of a premature infant who at birth presented a large, fluctuating swelling in the occipitoparietal region. The infant lived for twenty-four hours. At necropsy, the swelling was found to be due to the accumulation of about 300 cc. of a bloody, purulent fluid. There was a perforation, about 6 mm. in diameter in the anterior fontanel. The pus continued through this opening into the cavity of the skull, where it had caused a complete separation of the dura mater from the left parietal and frontal bones. The brain was transformed into a soft sac covered with the hemorrhagic leptomeningi and filled with a fluid similar to that found underneath the scalp. The cortex of the brain was reduced to a thin membrane. No micro-organisms could be demonstrated in the purulent fluid.

The mother was suffering from a preeclamptic toxemia. In cases of eclampsia, hemorrhagic and inflammatory lesions of the brain of the infant are sometimes found. In the case described, there seems to be a combination of congenital hydrocephalus with an hemorrhagic encephalitis, leading to the formation of pyohematocephalus. The pyocephalus apparently had broken through the anterior fontanel, causing an accumulation of the exudate between scalp and bone.

The last case demonstrates an early generalization of tuberculosis in a child, aged 3 years. Besides a diffuse caseation of the entire upper pulmonary lobe, of the right lung, there were numerous miliary tubercles in the liver, spleen, kidneys and leptomeninges.

NEPHROSIS. DR. JOSEPH K. CALVIN.

Three cases of typical lipoid nephrosis presented the cardinal symptoms of marked edema, albuminuria, cholesteremia, absence of blood in the urine, normal blood pressure and lack of increase in the nonprotein nitrogen content of the blood. The ages of the children were 3, 5 and 8 years, respectively.

In the first case the trouble followed a slight infection of the upper respiratory tract but repeated x-ray examinations of the nasal sinuses did not reveal any foci of infection. The second patient had a definite maxillary sinus infection which is being treated at present. The third case which is of two years' duration followed a bronchopneumonia. None of the children appears acutely ill. They have eaten well and have been fairly comfortable and playful in spite of the extreme edema. This is the only conditon in which so much edema could exist without the child

seeming extremely ill. The edema fluctuated widely from time to time inversely as the output of urine, the patient occasionally losing or gaining as much as 10 pounds (4.5 Kg.) in a week, in spite of various methods of treatment. Large doses of thyroid and ammonium chloride, high protein diets, laxatives, reduction of fluid intake, low salt intake, injections of foreign protein and urine and vegetable diuretics were tried, but resulted in only temporary if any benefit. It was interesting to note that the cholesteremia varied directly with the edema.

At times the edema seemed to have disappeared. The intradermal saline wheal, however, was still absorbed rapidly (within one-half hour) and the cholesterol content of the blood remained somewhat above normal, indicating that a latent edema persisted even when the patient apparently had recovered. Soon the edema would become manifest and the weight would increase again.

ATYPICAL VINCENT'S ANGINA. DR. C. K. STULIK, JR.

A child had swelling of the jaw for two weeks, experiencing pain and inability to open the mouth; the pain gradually migrated from the right to the left side. The patient was admitted to the hospital on October 11. At that time, there was marked sloughing of the gums, with loss of the lower incisors. There was much green, purulent material about the mouth and what appeared to be an alveolar abscess at the base of the lower molars. A hard, red, indurated mass then developed in both jaws. This looked like a beginning noma, and had the odor of gangrene. The treatment consisted of hourly lavage with peroxide. The culture gave a negative reaction at first; finally, fusiform bacilli with spirochetes or spirillae were found after anaerobic culture.

On admission to the hospital, the patient had a temperature of 101 F.; the red cells numbered 4,900,000, the white cells 9,000; the hemoglobin amounted to 90 per cent. Lavage with peroxide cleared up the conditon quickly, although the gum remained deeply indurated. The swelling of the jaw gradually subsided.

The diagnosis considered was that of an osteomyelitis of the jaw, and atypical Vincent's angina based on a primary alveolar abscess. The ordinary internal treatment with potassium chlorate was employed, and the child also received sulpharsphenamine, but the lavage with peroxide was apparently the most effective measure in this case.

ENDOCARDITIS: SUBACUTE, BACTERIAL. DR. P. ROSENBLUM.

A girl, aged 10 years, was admitted to the hospital in August, during an attack of acute endocarditis. There was a history of illness during the entire summer, with repeated sore throat and pain in the various joints of the body. The patient remained in the hospital for two weeks and went home against advice. She returned on September 10, with the history that three days previously she had suddenly developed paralysis of the right arm and leg and the right side of the face, with aphasia. The temperature was septic, running up to 104 F. The blood culture on three different occasions was negative. At the time of presentation, the patient was markedly anemic, with a café au lait color. The spleen was enlarged. There were only occasional petechiae, which were seen best in the conjunctivae. There are none present at this time. The spleen is not as large as it occasionally appears in the subacute bacterial cases. The urine gives a negative reaction.

A child, aged 2 years, under observation at present, has had for some time a septic temperature, a systolic murmur and enlargement of the heart, a hemiplegia similar to that in the present case suddenly developed. The child has both a mitral and an aortic lesion, the type of case most prone to develop with subacute bacterial endocarditis. Such conditions are not common in young children.

A CASE FOR DIAGNOSIS. DR. BLATT.

In June, 1927, a colored boy, aged 5 years, had whooping cough which persisted until September of that year. He came into the hospital on Sept. 4, 1928, with

the history that three months before, his mother noticed that his eyes were crossed, that he walked with a limp on the right side and that he had intense headache and vomiting. The condition persisted for about three weeks and disappeared, except for the limp and the crossed eyes. He was taken to another hospital, where a diagnosis of blindness in one eye was made.

On admission to the hospital, the child did not have an elevated temperature. The pupils were much more widely dilated than on presentation. A superficial examination showed that the pupils apparently did not react to light. Neither Babinski nor patellar reflexes could be obtained. Subsequent examination disclosed a light reflex in both eyes; furthermore, there were crossed light reflexes, a light put on the blind left eye producing contraction in the right pupil. The spinal fluid was under increased pressure, and showed 120 cells per cubic centimeter. It was always negative for tubercle bacilli, although centrifugated for ninety minutes. Three Wassermann tests of the blood and spinal fluid of the child and one on the mother gave negative reactions. The fluid showed increased globulin, and positive reactions to the Noone-Apelt and Ross-Jones tests. The sugar content of the spinal fluid was normal. The sulphosalicylic acid and mercuric chloride test of the spinal fluid showed tuberculosis. The Lange test showed a curve in the tuberculous area. The Pirquet test gave decidedly positive results.

A point of interest is the localization of the lesion. It is obviously anterior to the chiasm, since a crossed pupillary reflex is not present on the left side. Moderately choked disk and optic neuritis were reported three times by specialists. Inoculation of a guinea-pig made ten days before presentation continues to give negative results. A roentgenogram of the sella turcica showed a normal condition. There is infiltration of the hilum, but the temperature is not elevated and the condition of the patient is not becoming worse. The diagnosis lies between syphilis, meningeal tuberculosis en bloc, tuberculoma and tumor.

FOOD IRRADIATION. PROF. H. STEENBOCK.

The general proposition of the irradiation of food was brought to the attention of the author by some experiments on the calcium balance in a goat, under various dietary conditions. These experiments were carried out in 1913, but due to the extensive program of experimentation in progress the data were not tested completely until 1923. In 1923, as a result of work on growth carried out at the Lister Institute, the diets of rats which had ceased to grow were exposed to ultraviolet light. It was found that irradiation imparted to these diets or even to the tissues of the animals the property not only of inducing and maintaining growth, but of producing an increase in the ash content of the skeleton with concomitant healing of rachitic lesions. These experiments were elaborated on with the result that practically all food substances except dextrose, salts and water were found capable of being activated by irradiation.

Later it was found that the activity could not be induced in oils and fats, but rather in the unsaponifiable constituents which they contained, specifically, in the sterol fraction. Hess and Windaus, and Rosenheim and Webster found that not all sterols, but apparently only ergosterol, when irradiated, represented the potent agent.

It thus came about that by dietary treatment, the means were available to prevent rickets and to cure rickets and analogous conditions of deficient calcification of the skeleton. The possible explanation was furnished for the activity resident in cod liver oil. It has recently developed, however, that ergosterol administered in excessive doses, approximately in nearly 1,000 times the therapeutic dose, is capable of exerting a toxic action. This has necessitated the careful control of the treatment of foods and medicinals, in order that harmful effects may be prevented.

This is the problem which the Wisconsin Alumni Research Foundation has set for itself, because this organization is in possession of patients covering the process of irradiation. It is considered possible, at present, that by the judicious use of foods and medicinals, treated by the ultraviolet rays, the public may derive the benefit of this discovery without any hazards.

DISCUSSION

DR. MAURICE BLATT: The subject which Dr. Steenbock has discussed is one of extreme interest to physicians and to the public. The society is honored and deeply grateful to this scientist for his most interesting and instructive address. The responsibility for the health of the babies in this community lies with the members of this society. It is our duty to advise and suggest medical treatment. In view of the fact that there is still some question as to the exact dosage and incidental effects of irradiated foods, I am calling on Dr. Julius Hess to discuss the situation.

DR. JULIUS H. HESS: My impression is that the Wisconsin Research Foundation has already granted or is preparing to grant licenses to several firms to use that patented process which it controls for the purpose of irradiating food and medicinal products. Believing that there are real dangers in overdosage, I am taking the liberty of quoting from the literature of two firms which are prepared to enter the market at this time with products containing irradiated ergosterol.

In the following discussion, the two products are spoken of as Product A and Product B. Descriptive of Product A, the following statement appears: "each minim of . . . is equivalent in Vitamin D potency to 1½ drachms of cod liver oil. The suggested dose for infants is 1 to 5 drops daily." On the carton enclosing the product as it is to be marketed there appears the statement "1 drop equals in vitamin D potency 1½ teaspoonfuls of cod liver oil." I wish to direct attention to the fact that a drop of this product obtained from the dropper furnished with the bottle averages but little more than one-half minim.

In the booklet describing Product B, the dose recommended for infants and young children is from 5 to 10 drops. According to the statement on the carton, product A is standardized to 100 times the antirachitic potency of high grade cod liver oil, while product B is standardized to approximately 200 times the antirachitic potency of standardized cod liver oil. If these figures permit of comparison, the amount of irradiated ergosterol contained in product A is much less than that contained in product B; yet the dose recommended is only about one-half as much. It is my impression that these recommendations are most confusing and create a marked uncertainty as to the dosage. In fact, samples of products A and B recently tested show that the activity in B is approximately 16 times that in A.

The difference in methods of standardization add to the confusion surrounding the administration of the two products: One is standarized on the basis of a definite number of milligrams of irradiated ergosterol per dose. In the other product, the great variation in the capacity of ergosterol to assume antirachitic activity, causes the rejection of such a standardization as impracticable; in this method each batch is individually tested by animal experimentation.

A personal communication from one of the producers states: "We should say that irradiated ergosterol must be considered as an extremely potent drug such as tincture of digitalis and that small doses are very beneficial and large doses are toxic." They state further that irradiated ergosterol should be prescribed only by physicians and should not be placed under any circumstances at the disposal of the general public. Control of the product in this way seems impossible if the present plans for marketing are adopted.

The published literature frequently refers to variation in the effects of doses recommended by manufacturers for normal infants fed prophylactically and in the effects of similar amounts fed to rachitic infants. This applies especially to the not infrequent development of the symptoms of hypercalcemia in normal infants. Clinical reports show far less evidence of this condition in rachitic infants. These observations are worthy of serious consideration. The literature also contains references to the cumulative action of irradiated ergosterol as evidenced by the constancy of a high percentage of calcium and phosphorus in the blood.

Appreciating the difficulties of standardizing the dosage and estimating the therapeutic effect on normal infants prophylactically fed and rachitic infants therapeutically treated with irradiated ergosterol does it seem reasonably safe

to flood the market with more complex irradiated food products, such as whole canned milk, dried milk, cereals and yeast. The head of the department of experimental medicine in one of the firms which was promised a license by the Foundation to irradiate ergosterol, stated that this firm believed that they required at least from six to twelve months more to evaluate their product properly.

Of even greater interest may be the recent announcement of the producers of product A that they will recall all commercial shipments already made of their irradiated ergosterol and that they will withhold it from the market until the prophylactic and therapeutic indications and the dosage are established by further clinical research.

PROF. F. C. KOCH: I think that I can subscribe to practically everything that Dr. Hess has said, and I am also pleased with the attitude of Professor Steenbock. He has given us ample warning of the dangers that are possible in the use of the irradiated drugs, pure substances or foods. I think it is safe to say that if the irradiation of foods, or even of supposedly pure substances as ergot or cholesterol, or modified cholesterol, is practiced without full control, we are certain to obtain substances that will vary in potency in rickets, and also may add toxic substances. There is danger of that and I do not think that we should take a chance until we have carefully investigated all of the phases. It is much better to try to prevent these errors than to do the harm and try to correct them later.

One question is that of the purity of ergosterol itself. The recent literature indicates that at present probably really pure ergosterol is not being used. English workers have found zymosterol present in ergosterol, and other workers claim to have found still other sterols. This shows the many details that are involved in the intelligent use of this material. Unquestionably, toxic effects have been produced.

Book Reviews

THE DAILY HEALTH BUILDER. By C. WARD CRAMPTON. Price, $1.50. Pp. 161, with illustrations. New York: C. P. Putnam's Sons, 1928.

"For it is only by muscular work that we can strengthen the heart, lungs, stomach, liver, intestines and endocrine organs.

"This (referring to muscular exercise) is the only way to get a real appetite and the only incentive the body has to digest a good meal.

"A well used stomach cannot have dyspepsia, an active set of intestines cannot poison the body.

"If you wish your liver well and desire to keep it comfortably on the right side where it belongs, give it its daily massage.

"Muscular exercise can therefore be made organic exercise. In no other way can we make the organs strong and in no other way can we keep them strong."

These statements are not advertisements for patent medicine. They are taken from a book called "The Daily Health Builder," written by C. Ward Crampton. It is unfortunate that in order to get down to the level of his lay readers, an able physician who is an expert in his specialty should place himself in such an equivocal position. There is much in this book on physical exercise, that is of practical value to the physician as well as the layman but it is lost in the large amount of exaggerated and overenthusiastic verbiage.

SPASMOPHILIA. By E. C. WRIGHTSMAN, M.D. Pp. 155, with 16 photographs. Boston: Richard G. Badger, 1928.

The title of this book is rather unfortunate as only the first sixty-two pages deal with spasmophilia. The first part is devoted to a discussion of rickets and spasmophilia. The etiology, types, differential diagnosis and treatment are given in full. The section on spasmophilia is well covered with frequent reference to cases in the author's experience. Wrightsman believes that in many cases in which spasmophilia is not shown clinically, and in which the diagnosis is apparently limited to epilepsy a treatment for spasmophilia is indicated. The second part of the book is devoted entirely to infant feeding. A simple, concise resumé of the more commonly used foods in infancy is given in as readable a manner as will be found in more pretentious textbooks entirely devoted to infant feeding.

TABLE FOR RECKONING INFANT NOURISHMENT ACCORDING TO THE NEM SYSTEM. By J. V. LUKACS and A. EBEL, M.D. Price, 4.20 marks.

This book as the name indicates, contains a table for use in reckoning food values according to the Nem System. It refers to various foods which are used extensively in Germany. For one who uses this system the table will probably be of much value.

Directory of Pediatric Societies

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SECTION ON DISEASES OF CHILDREN

Chairman: Dr. W. A. Mulherin, 753 Broad St., Augusta, Ga.
Secretary: Dr. C. A. Aldrich, 545 Lincoln Ave., Winnetka, Ill.
Place: Portland, Ore. Time: July 8-12, 1929.

AMERICAN PEDIATRIC SOCIETY

President: Dr. Henry L. K. Shaw, 142 Washington Ave., Albany, N. Y.
Secretary: Dr. Howard Childs Carpenter, 1805 Spruce St., Philadelphia.
Place: St. Louis. Time: 1929.

THE ASSOCIATION OF AMERICAN TEACHERS OF THE DISEASES OF CHILDREN

President: Dr. Paul W. Emerson, 86 Bay State Road, Boston.
Secretary: Dr. Ralph M. Tyson, 1527 Pine St., Philadelphia.
Place: Portland, Ore. Time: July 8-12, 1929.

AMERICAN CHILD HEALTH ASSOCIATION

President: Hon. Herbert Hoover, 370 Seventh Ave., New York.
Secretary: Dr. Philip Van Ingen, 370 Seventh Ave., New York.

CANADIAN SOCIETY FOR THE STUDY OF DISEASES OF CHILDREN

President: Dr. Thomas Crossan Clark, 51 Herkimer St., Hamilton, Ont.
Secretary-Treasurer: Dr. Frank H. Boone, 164 James St. S., Hamilton, Ont.

SECTIONAL

CENTRAL STATES PEDIATRIC SOCIETY

President: Dr. J. Gurney Taylor, 120 E. Wisconsin St., Milwaukee.
Secretary: Dr. A. H. Parmelee, 310 S. Michigan Ave., Chicago.
Place: Milwaukee. Time: October, 1929.

SECTION ON PEDIATRICS OF SOUTHERN MEDICAL ASSOCIATION

Chairman: Dr. E. C. Mitchell, 1073 Madison Ave., Memphis, Tenn.
Secretary: Dr. A. J. Waring, De Renne Apts., Savannah, Ga.

LOCAL

NORTHERN CALIFORNIA PEDIATRIC SOCIETY

President: Dr. W. L. Channell, Medical Bldg., Oakland, Calif.
Secretary: Dr. J. E. Parrott, Medico-Dental Bldg., San Francisco.
Place: Various Teaching Schools. Time: Monthly.

SOUTHWESTERN PEDIATRIC SOCIETY

President: Dr. George P. Laton, 1136 W. 6th St., Los Angeles.
Secretary: Dr. William Sidney Bowers, 1136 W. 6th St., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

THE ROCKY MOUNTAIN PEDIATRIC SOCIETY

President: Dr. W. Wiley Jones, Majestic Bldg., Denver.
Secretary: Dr. Berryman Green, Republic Bldg., Denver.
Place: Children's Hospital, Denver. Time: Third Saturday of each month, 2:30 p. m., September to May, inclusive.

GEORGIA PEDIATRIC SOCIETY

President: Dr. W. N. Adkins, Medical Arts Bldg., Atlanta.
Secretary and Treasurer: Dr. E. N. Gleaton, 212 E. Gaston St., Savannah.

PEDIATRIC SECTION OF FULTON COUNTY MEDICAL SOCIETY, ATLANTA, GA.

Chairman: Dr. Willis Ragan, Medical Arts Bldg., Atlanta.
Secretary: Dr. Lee Bivings, Exchange Bldg., Atlanta.
Place: Academy of Medicine, 32 Howard St., Atlanta. Time: Second Thursday of each month from October to April, at 8 p. m.

NEW ENGLAND PEDIATRIC SOCIETY

Chairman: Dr. William W. Howell, 279 Clarendon St., Boston.
Secretary: Dr. Randolph K. Byers, 66 Commonwealth Ave., Boston.
Place: Boston Medical Library. Time: Second Friday of each month.

CHICAGO PEDIATRIC SOCIETY

President: Dr. Maurice Blatt, 185 N. Wabash Ave., Chicago.
Secretary: Dr. J. K. Calvin, 104 S. Michigan Ave., Chicago.
Place: City Club. Time: Third Tuesday of each month.

LOUISIANA STATE PEDIATRIC SOCIETY

President: Dr. L. R. De Buys, 1417 Delachaise St., New Orleans.
Secretary-Treasurer: Dr. C. T. Williams, 7401 Burthe St., New Orleans.

DETROIT PEDIATRIC SOCIETY

President: Dr. M. Boyd Kay, 10 Peterboro St., Detroit.
Secretary: Dr. Charles A. Wilson, 71 E. Ferry St., Detroit.
Place: Children's Hospital of Michigan. Time: No fixed date; approximately once a month.

NORTHWESTERN PEDIATRIC SOCIETY

President: Dr. Ray Shannon, Lowry Bldg., St. Paul.
Secretary: Dr. E. S. Platou, 730 La Salle Bldg., Minneapolis.
Place: University Campus and Rochester. Time: Winter, Spring, Summer, Fall.

ST. LOUIS PEDIATRIC SOCIETY

President: Dr. Park J. White, Beaumont Bldg., St. Louis.
Secretary-Treasurer: Dr. Ralph L. Cook, 508 N. Grand Blvd., St. Louis.
Place: St. Louis Children's Hospital. Time: At least once a year and contingent thereafter on the arrangement of a suitable program.

NEBRASKA-IOWA PEDIATRIC SOCIETY

President: Dr. Floyd Clarke, City Nat'l Bank Bldg., Omaha.
Secretary: Dr. R. B. Eldredge, Medical Arts Bldg., Omaha.
Place: Add-Sell Restaurant. Time: Second Thursday of each month from October to May, inclusive, 6 p. m.

BROOKLYN PEDIATRIC SOCIETY

President: Dr. Louis M. Ruderman, 961 Eastern Parkway, Brooklyn.
Secretary: Dr. Joseph F. Paulonis, 1357 Bushwick Ave., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Last Wednesday of each month, except June, July and August.

BRONX PEDIATRIC SOCIETY

President: Dr. William Hinz, 1964 Grand Concourse, New York.
Secretary: Dr. L. H. Barenberg, 1749 Grand Concourse, New York.
Place: Concourse Plaza, 161st St. and Grand Concourse, New York.
Time: Second Wednesday of each month, except June, July, August and September.

CENTRAL NEW YORK PEDIATRIC CLUB

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various Cities in New York. Time: Fourth Thursday of October, January and April.

PEDIATRIC SECTION OF THE NEW YORK ACADEMY OF MEDICINE

President: Dr. Stafford McLean, 17 East 71st St., New York.
Secretary: Dr. F. Elmer Johnson, 300 West End Ave., New York.
Place: New York Academy of Medicine, 2 East 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

ROCHESTER PEDIATRIC SOCIETY

President: Dr. Paul W. Beaven, 26 S. Goodman St., Rochester, N. Y.
Secretary: Dr. Edwin R. Reynolds, 1620 St. Paul St., Rochester, N. Y.
Place: Arranged by Program Committee. Time: First Friday of each month from October to May.

THE PEDIATRIC SECTION OF THE ACADEMY OF MEDICINE OF CLEVELAND

Chairman: Dr. C. W. Wyckoff, 8314 Euclid Ave., Cleveland.
Secretary: Dr. C. L. Ruggles, 10616 Euclid Ave., Cleveland.
Place: 2009 Adelbert Road. Time: Four meetings, from September to May.

PHILADELPHIA PEDIATRIC SOCIETY

President: Dr. Edward L. Bauer, Jefferson Medical College, Philadelphia.
Secretary: Dr. John Porter Scott, 2040 Pine St., Philadelphia.
Place: College of Physicians, 19 S. 22nd St., Philadelphia. Time: Second Tuesday of each month from October to June, inclusive.

PITTSBURGH PEDIATRIC SOCIETY

President: Dr. Zaccheus R. Scott, Westinghouse Bldg., Pittsburgh.
Secretary: Dr. Theodore C. Elterich, Highland Bldg., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months.

MEMPHIS PEDIATRIC SOCIETY

President: Dr. W. D. Blue, 1024 Madison Ave., Memphis, Tenn.
Secretary: Dr. Gilbert J. Levy, 899 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month.

TEXAS PEDIATRIC SOCIETY

President: Dr. Edwin G. Schwarz, Medical Arts Bldg., Fort Worth.
Secretary-Treasurer: Dr. Ramsey Moore, Medical Arts Bldg., Dallas.

RICHMOND PEDIATRIC SOCIETY

President: Dr. T. D. Jones, Medical Arts Bldg., Richmond, Va.
Secretary: Dr. W. Ambrose McGee, West End Medical Bldg., 2618 Grove Ave., Richmond, Va.
Place: Westmoreland Club, 601 E. Grace St., Richmond, Va.
Time: First Thursday of each month (other than during the summer).

VIRGINIA PEDIATRIC SOCIETY

President: Dr. Charles E. Conrad, Harrisonburg.
Secretary: Dr. William B. McIlwaine, Petersburg.

NORTH PACIFIC PEDIATRIC SOCIETY

President: Dr. E. D. Carder, 736 Granville St., Vancouver, B. C.
Secretary and Treasurer: Dr. George A. Lamont, 736 Granville St., Vancouver, B. C.

SEATTLE PEDIATRIC SOCIETY

President: Dr. Arthur H. Gray, Lumber Exchange Bldg., Seattle.
Secretary: Dr. Armin Rembe, Stimson Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, at 7 p. m.

MILWAUKEE PEDIATRIC SOCIETY

President: Dr. A. L. Kastner, 120 E. Wisconsin St., Milwaukee.
Secretary: Dr. F. R. Janney, 418 E. North Ave., Milwaukee.
Place: Children's Hospital, Milwaukee. Time: Second Wednesday of each alternate month, beginning with February.

PEDIATRIC SECTION, ACADEMY OF MEDICINE, TORONTO

Chairman: Dr. F. R. Hassard, 1361 King St. West, Toronto.
Secretary: Dr. G. A. Davis, 12 Belsize Dr., Toronto.
Time: November 17, December 15, February 16 and March 15.